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(54) **Ameliorant or remedy for symptoms caused by Ischemic diseases and Phenylpiperidine compounds useful therefor**

VERBESSERUNG ODER HEILUNG VON DURCH ISCHÄMISCHEN KRANKHEITEN HERVORGERUFENEN SYMTOMEN UND DAFÜR VERWENDBARE PHENYLPIPERIDINVERBINGUNGEN

AMELIORANT OU REMEDE CONTRE DES SYMPTOMES PROVOQUES PAR DES MALADIES ISCHEMIQUES ET COMPOSES PHENYLPIPERIDINIQUES UTILES A CET EFFET

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(56) References cited:

EP-A- 0 347 305	**WO-A-93/11107**
WO-A-93/22302	**WO-A-95/03291**
WO-A-95/11238	**WO-A-95/11240**
JP-A- 1 047 776	**JP-A- 2 218 651**
JP-A- 2 225 464	**JP-A- 53 095 963**
JP-T- 3 505 456	**US-A- 4 241 071**

- **CHEMICAL ABSTRACTS, vol. 116, no. 11, 16 March 1992 Columbus, Ohio, US; abstract no. 106319q, page 782; XP002021181 & ES-A-2 020 127 (FERRER INTERNATIONAL S. A.) 16 July 1991**
- **JOURNAL OF MEDICAL CHEMISTRY, 1979, Vol. 22, No. 11, LAURENCE L. MARTIN et al., pp. 1347-1354.**

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Description

TECHNICAL FIELD

[0001] The present invention relates to medicaments for the alleviation or treatment of symptoms based on ischemic diseases, for example, cerebral infarction, intracerebral hemorrhage, transient ischemic attack, subarachnoid hemorrhage, head trauma, after effects of brain surgery, after effects of cerebral arteriosclerosis and other cerebrovascular disorders, or variant angina, unstable angina, myocardial infarction, cardiovascular system disorders accompanying surgery for revascularization by PTCA/PTCR/CABG etc., malignant arrhythmia, and other myocardial ischemia-reperfusion injury, and further symptoms due to disorders of transplanted organs at the time of organ transplants, temporary blockage of the blood flow in organs at the time of surgery, etc. or symptoms derived from seizures, epilepsy, migraine, etc.

[0002] The present invention further relates to novel piperidine derivatives, tetrahydropyridine derivatives, piperazinodiphenylether derivatives, and piperazinodiphenylmethane derivatives useful for the alleviation or treatment of symptoms based on aforementioned ischemic diseases and intermediates for the synthesis of aforementioned compounds.

BACKGROUND ART

[0003] In cellular disorders caused by advanced ischemia, the depletion of ATP, the fall in the pH in the cells, and the destruction of the mechanism for maintenance of the energy-dependent ion homeostasis inside and outside the cell cause the accumulation of a large amount of intracellular divalent Ca ions (Ca^{2+}) (Ca^{2+} overload). It is believed that the Ca^{2+} overload causes functional disorders in the mitochondria and randomly activates various enzyme reactions and invites further Ca^{2+} overload to cause a repeated vicious cycle and in the end causes irreparable damage to the cell wall and cell death [F. B. Meyer: Brain Res. Rev., 14, 227 (1989); E. Boddeke et al.: Trends Pharmacol. Sci., 10, 397 (1989)].

[0004] Medicament for suppressing cytotoxic Ca^{2+} overload are considered useful for the alleviation or treatment of various ischemic diseases, for example, cerebral infarction, intracerebral hemorrhage, transient ischemic attack, subarachnoid hemorrhage, head trauma, after effects of brain surgery, after effects of cerebral arteriosclerosis and other cerebrovascular disorders, or variant angina, unstable angina, myocardial infarction, cardiovascular system disorders accompanying surgery for revascularization by PTCA/PTCR/CABG etc., malignant arrhythmia and myocardial ischemia-reperfusion injury, and further disorders of transplanted organs at the time of organ transplants and temporary blockage of the blood flow in organs at the time of surgery, however, no medicament with sufficient activity has yet been obtained.

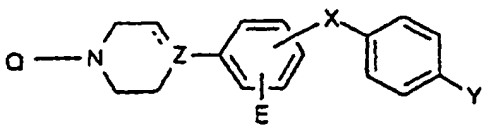
DISCLOSURE OF INVENTION

[0005] In consideration of the state of the prior art, the objective of the present invention is to provide medicaments which have the powerful action of suppressing cytotoxic Ca^{2+} overload for the alleviation and treatment without side effects of symptoms based on ischemic diseases or symptoms derived from seizures, epilepsy, migraine, etc.

[0006] Another objective of the present invention is to provide novel compounds and their salts useful as the medicaments and intermediates for synthesizing the same.

[0007] The present inventors screened compounds by evaluating the inhibitory effects on the non-L type Ca^{2+} channel and Na^{+} channel reported to be involved in the mechanism of cause of the Ca^{2+} overload (P. J. Pauwels et al., Life Science, 48, 1881 (1991)].

[0008] As a result, we found that compounds of the general formula (I):



(I)

wherein, Q represents a group having the formula:

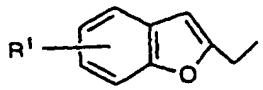
R-A-B-

in which R represents a hydrogen atom, substituted or unsubstituted phenyl group, substituted or unsubstituted phenoxy group, or substituted or unsubstituted benzoyl group,

A represents a connecting bond, a cycloalkylene group, an alkenylene group which may be substituted by a lower alkyl group, a dialkoxymethylene group, or a hydroxyiminomethylene group, and

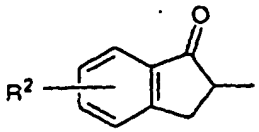
B represents an alkylene group which may be substituted by a hydroxyl group or an alkoxy group;

a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, an alkyl group which may be substituted by a halogen atom, an alkoxy group, or a hydroxyl group; or

a group having the formula:



in which R^2 represents a hydrogen atom, a halogen atom, an alkyl group which may be substituted by a halogen atom, an alkoxy group, or a hydroxyl group;

X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring being in a para position,

E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, an alkoxy group, or an alkyl group which may be substituted by a halogen atom,

the dotted line shows the presence or absence of a bond, when said dotted line shows the presence of a bond, Z represents a carbon atom, and when said dotted line shows the absence of a bond, Z represents CH or a nitrogen atom have powerful inhibitory actions on one type of the non-L type Ca^{2+} channel, that is, the T-type Ca^{2+} channel, and Na^+ channel and are effective in various types of animal disease models and thereby completed the present invention.

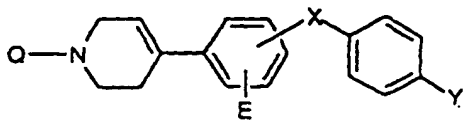
BEST MODE FOR CARRYING OUT THE INVENTION

[0009] Flunarizine which is used as an agent for improvement of the brain circulation [P. J. Pauwels et al.; Life Science, 48, 1881 (1991); G. E. Billman; Eur. J. Pharmacol., 212, 231 (1992)] suffers from the problem that it causes as a side effect the onset of symptoms of Parkinson's disease due to its action of blocking dopamine D_2 receptors. This is a major defect in its use. The compounds of the general formula (I) of the present invention, however, were found to have an extremely low affinity for the dopamine D_2 receptors causing the side effects of flunarizine.

[0010] In the present invention, ischemic diseases include cerebral ischemic diseases, for example, cerebral infarction, intracerebral hemorrhage, transient ischemic attack, subarachnoid hemorrhage, head trauma, after effects of brain surgery, after effects of cerebral arteriosclerosis, and other functional and organic diseases of the brain, ischemic cardiac diseases, for example, variant angina, unstable angina, myocardial infarction, cardiovascular system disorders accompanying surgery for revascularization by PTCA/PTCR/CABG etc., malignant arrhythmia and other myocardial ischemia-reperfusion injury, and also disorders of transplanted organs at the time of organ transplants, and temporary blockage of the blood flow in organs at the time of surgery.

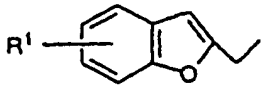
[0011] The compounds having the general formula (I) of the present invention include compounds of the following general formulas (Ia), (Ib), (Ic), (Id), (Ie), (If), (Ig), (Ih), and (Ii).

[0012] In the general formula (Ia):

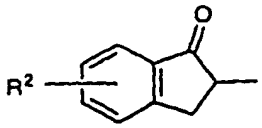


(Ia)

wherein, Q represents a group having the formula R-A-B-, the formula:



or the formula:



and A, B, E, R, R^1, R^2, X, and Y are as defined above, preferable examples of substituents for the substituted or unsubstituted phenyl group, substituted or unsubstituted phenoxy group, or substituted or unsubstituted benzoyl group represented by R include a halogen atom such as a fluorine atom, a chlorine atom and a bromine atom, a hydroxyl group, a C_1 - C_5 alkokyl group which may be branched such as a methoxy group and an ethoxy group, and a C_1 - C_5 alkyl group which may be branched and may be substituted by a halogen atom, such as a methyl group, an ethyl group and a trifluoromethyl group. Examples of a halogen atom of the C_1 - C_5 alkyl group which may be branched and may be substituted by a halogen atom include a fluorine atom, a chlorine atom, and a bromine atom.

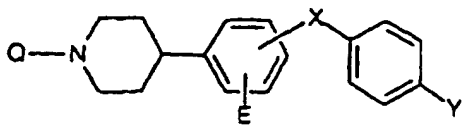
[0013] Examples of the cycloalkylene group represented by A include a 1,1-cyclopropylene group, a 1,2-cyclopropylene group, a 1,1-cyclobutylene group, a 1,1-cyclopentylene group, a 1,1-cyclohexylene group, etc., preferably a C_3 - C_6 cycloalkylene group, particularly preferably a 1,1-cyclopropylene group or a 1,2-cyclopropylene group; preferable examples of the alkenylene group of the alkenylene group which may be substituted by a lower alkyl group include, preferably a C_2 - C_4 alkenylene group such as a vinylene group and a butadienylene group, particularly preferably a vinylene group; preferable examples of the lower alkyl group of the alkenylene group which may be substituted by a lower alkyl group include a methyl group, ethyl group, propyl group, or isopropyl group; preferable examples of the alkoxyl group of the dialkoxymethylene group include a C_1 - C_5 alkoxy group which may be branched such as a methoxy group and an ethoxy group; and, further, the dialkoxymethylene group may be a cyclic acetal such as an ethylene acetal.

[0014] Preferable examples of the alkylene group of the alkylene group which may be substituted by a hydroxyl group or an alkoxy group represented by B include preferably a C_1 - C_6 alkylene group which may be branched such as a methylene group, dimethylene group, trimethylene group, tetramethylene group, methylmethylene group, propylene group, cyclopropylmethylene group, etc., particularly preferably a methylene group, dimethylene group, tetramethylene group, or cyclopropylmethylene group. Preferable examples of the alkoxy group of the alkylene group which may be substituted by an alkoxy group include a C_1 - C_5 alkoxy group which may be branched, such as a methoxy group and an ethoxy group.

[0015] Preferable examples of the halogen atom represented by R^1 or R^2 include a fluorine atom, a chlorine atom, or a bromine atom; preferable examples of the alkyl group which may be substituted by a halogen include a C_1 - C_5 alkyl group which may be branched, such as a methyl group, an ethyl group, and a trifluoromethyl group; and preferable examples of the alkoxy group include a C_1 - C_5 alkoxy group which may be branched, such as a methoxy group and an ethoxy group. Preferable examples of the halogen atom of the alkyl group which may be substituted by a halogen atom include a fluorine atom, chlorine atom, and bromine atom.

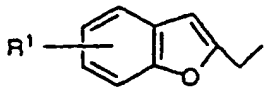
[0016] Preferable examples of the halogen atom represented by E or Y include a fluorine atom, chlorine atom, and bromine atom preferable examples of the alkoxy group include a C_1 - C_5 alkoxy group which may be branched, such as a methoxy group and an ethoxy group; and preferable examples of the alkyl group which may be substituted by a halogen atom include a C_1 - C_5 alkyl group which may be branched, such as a methyl group, ethyl group, trifluoromethyl group. Examples of the halogen atom of the alkyl group which may be substituted by a halogen atom include a fluorine atom, chlorine atom, and bromine atom.

[0017] In the general formula (Ib):

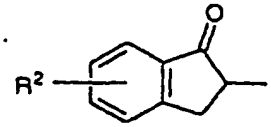


(Ib)

Q represents a group having the formula R-A-B-, the formula:



or the formula:



and A, B, E, R, R^1, R^2, X, and Y are as defined above, preferable examples of substituents for the substituted or unsubstituted phenyl group, substituted or unsubstituted phenoxy group, or substituted or unsubstituted benzoyl group represented by R include a halogen atom such as a fluorine atom, a chlorine atom and a bromine atom, a hydroxyl group, a C_1 - C_5 alkokyl group which may be branched such as a methoxy group and an ethoxy group, and a C_1 - C_5 alkyl group which may be branched and may be substituted by a halogen atom, such as a methyl group, an ethyl group and a trifluoromethyl group. Examples of a halogen atom of the C_1 - C_5 alkyl group which may be branched and may be substituted by a halogen atom include a fluorine atom, a chlorine atom, and a bromine atom.

[0018] Examples of the cycloalkylene group represented by A include a 1,1-cyclopropylene group, a 1,2-cyclopropylene group, a 1,1-cyclobutylene group, a 1,1-cyclopentylene group, a 1,1-cyclohexylene group, etc., preferably a C_3 - C_6 cycloalkylene group, particularly preferably a 1,1-cyclopropylene group or a 1,2-cyclopropylene group; preferable examples of the alkenylene group of the alkenylene group which may be substituted by a lower alkyl group include, preferably a C_2 - C_4 alkenylene group such as a vinylene group and a butadienylene group, particularly preferably a vinylene group; preferable examples of the lower alkyl group of the alkenylene group which may be substituted by a lower alkyl group include a methyl group, ethyl group, propyl group, or isopropyl group; preferable examples of the alkoxyl group of the dialkoxymethylene group include a C_1 - C_5 alkoxy group which may be branched such as a methoxy group and an ethoxy group; and, further, the dialkoxymethylene group may be a cyclic acetal such as an ethylene acetal.

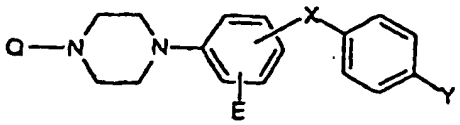
[0019] Preferable examples of the alkylene group of the alkylene group which may be substituted by a hydroxyl group or an alkoxy group represented by B include preferably a C_1 - C_6 alkylene group which may be branched such as a methylene group, dimethylene group, trimethylene group, tetramethylene group, methylmethylene group, propylene group, cyclopropylmethylene group, etc., particularly preferably a methylene group, dimethylene group, tetramethylene group, or cyclopropylmethylene group. Preferable examples of the alkoxy group of the alkylene group which may be substituted by an alkoxy group include a C_1 - C_5 alkoxy group which may be branched, such as a methoxy group and an ethoxy group.

[0020] Preferable examples of the halogen atom represented by R^1 or R^2 include a fluorine atom, a chlorine atom, or a bromine atom; preferable examples of the alkyl group which may be substituted by a halogen include C_1 - C_5 alkyl group which may be branched, such as a methyl group, an ethyl group, and a trifluoromethyl group; and preferable examples of the alkoxy group include a C_1 - C_5 alkoxy group which may be branched, such as a methoxy group and an ethoxy group. Preferable examples of the halogen atom of the alkyl group which may be substituted by a halogen atom include a fluorine atom, chlorine atom, and bromine atom.

[0021] Preferable examples of the halogen atom represented by E or Y include a fluorine atom, chlorine atom, and bromine atom, preferable examples of the alkoxy group include a C_1 - C_5 alkoxy group which may be branched, such as a methoxy group and an ethoxy group; and preferable examples of the alkyl group which may be substituted by a

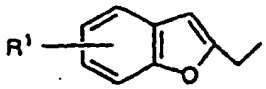
halogen atom include a C_1 - C_5 alkyl group which may be branched, such as a methyl group, ethyl group, trifluoromethyl group. Examples of the halogen atom of the alkyl group which may be substituted by a halogen atom include a fluorine atom, chlorine atom, and bromine atom.

[0022] In the general formula (Ic):

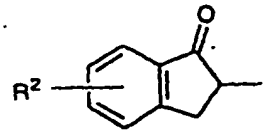


(Ic)

wherein, Q represents a group of the formula R-A-B-, the formula:



or the formula:



and A, B, E, R, R^1, R^2, X, and Y are as defined above, preferable examples of substituents for the substituted or unsubstituted phenyl group, substituted or unsubstituted phenoxy group, or substituted or unsubstituted benzoyl group represented by R include a halogen atom such as a fluorine atom, a chlorine atom and a bromine atom, a hydroxyl group, a C_1 - C_5 alkokyl group which may be branched such as a methoxy group and an ethoxy group, and a C_1 - C_5 alkyl group which may be branched and may be substituted by a halogen atom, such as a methyl group, an ethyl group and a trifluoromethyl group. Examples of a halogen atom of the C_1 - C_5 alkyl group which may be branched and may be substituted by a halogen atom include a fluorine atom, a chlorine atom, and a bromine atom.

[0023] Examples of the cycloalkylene group represented by A include a 1,1-cyclopropylene group, a 1,2-cyclopropylene group, a 1,1-cyclobutylene group, a 1,1-cyclopentylene group, a 1,1-cyclohexylene group, etc., preferably a C_3 - C_6 cycloalkylene group, particularly preferably a 1,1-cyclopropylene group or a 1,2-cyclopropylene group; preferable examples of the alkenylene group of the alkenylene group which may be substituted by a lower alkyl group include, preferably a C_2 - C_4 alkenylene group such as a vinylene group and a butadienylene group, particularly preferably a vinylene group; preferable examples of the lower alkyl group of the alkenylene group which may be substituted by a lower alkyl group include a methyl group, ethyl group, propyl group, or isopropyl group; preferable examples of the alkoxyl group of the dialkoxymethylene group include a C_1 - C_5 alkoxy group which may be branched such as a methoxy group and an ethoxy group; and, further, the dialkoxymethylene group may be a cyclic acetal such as an ethylene acetal.

[0024] Preferable examples of the alkylene group of the alkylene group which may be substituted by a hydroxyl group or an alkoxy group represented by B include preferably a C_1 - C_6 alkylene group which may be branched such as a methylene group, dimethylene group, trimethylene group, tetramethylene group, methylmethylene group, propylene group, cyclopropylmethylene group, etc., particularly preferably a methylene group, dimethylene group, tetramethylene group, or cyclopropylmethylene group. Preferable examples of the alkoxy group of the alkylene group which may be substituted by an alkoxy group include a C_1 - C_5 alkoxy group which may be branched, such as a methoxy group and an ethoxy group.

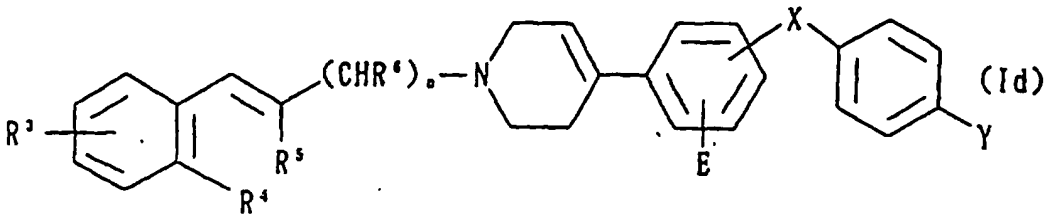
[0025] Preferable examples of the halogen atom represented by R^1 or R^2 include a fluorine atom, a chlorine atom, or a bromine atom; preferable examples of the alkyl group which may be substituted by a halogen include C_1 - C_5 alkyl group which may be branched, such as a methyl group, an ethyl group, and a trifluoromethyl group; and preferable examples of the alkoxy group include a C_1 - C_5 alkoxy group which may be branched, such as a methoxy group and an ethoxy group. Preferable examples of the halogen atom of the alkyl group which may be substituted by a halogen

atom include a fluorine atom, chlorine atom, and bromine atom.

[0026] Preferable examples of the halogen atom represented by E or Y include a fluorine atom, chlorine atom, and bromine atom, preferable examples of the alkoxy group include a C_1 - C_5 alkoxy group which may be branched, such as a methoxy group and an ethoxy group; and preferable examples of the alkyl group which may be substituted by a halogen atom include a C_1 - C_5 alkyl group which may be branched, such as a methyl group, ethyl group, trifluoromethyl group. Examples of the halogen atom of the alkyl group which may be substituted by a halogen atom include a fluorine atom, chlorine atom, and bromine atom. is

[0027] The substitution of X for the benzene ring is in a para position.

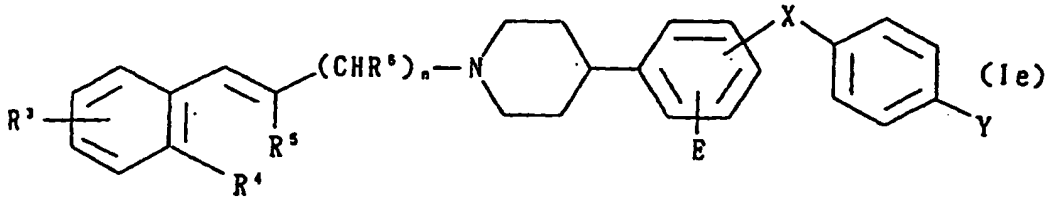
[0028] In the general formula (Id):



R^3 represents a hydrogen atom, a halogen atom, an alkyl group which may be substituted by a halogen atom, an alkoxy group, or a hydroxyl group, R^4 and R^5 are the same or different from each other and represent a hydrogen atom or a lower alkyl group, or R^4 and R^5 are taken together to represent -O-, R^6 represents a hydrogen atom, a hydroxyl group, an alkoxy group, or an alkyl group, n is an integer of 1 to 6, and E, X, and Y are as defined above,
preferable examples of the halogen atom represented by R^3 include a fluorine atom, a chlorine atom and a bromine atom; preferable examples of the alkyl group which may be substituted by a halogen atom include a C_1 - C_5 alkyl group which may be branched such as a methyl group, an ethyl group and a trifluoromethyl group; and preferable examples of the alkoxyl group include a C_1 - C_5 alkoxy group which may be branched such as a methoxy group and an ethoxy group. Examples of the halogen atom of the alkyl group which may be substituted by a halogen atom include a fluorine atom, a chlorine atom, and a bromine atom. Examples of the lower alkyl group represented by R^4 or R^5 include a methyl group, an ethyl group, a propyl group, and an isopropyl group. Preferable examples of the alkoxyl group represented by R^6 include a C_1 - C_5 alkoxyl group which may be branched such as a methoxy group and an ethoxy group; and preferable examples of the alkyl group include a C_1 - C_5 alkyl group which may be branched such as a methyl group, an ethyl group, and a propyl group.

[0029] Preferable examples of the integer shown by n include 1, 2, and 3.

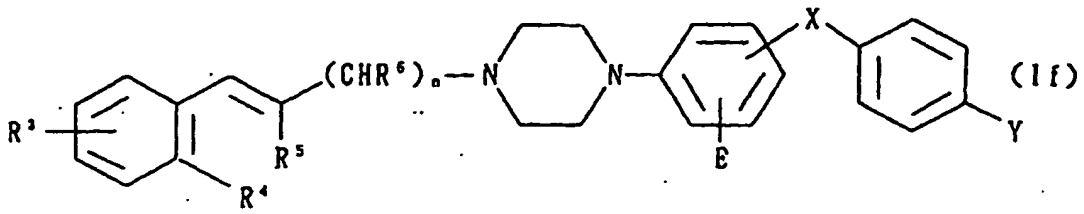
[0030] In the general formula (Ie):



wherein E, R^3, R^4, R^5, R^6, X, Y, and n are as defined above, preferable examples of the halogen atom represented by R^3 include a fluorine atom, a chlorine atom and a bromine atom; preferable examples of the alkyl group which may be substituted by a halogen atom include a C_1 - C_5 alkyl group which may be branched such as a methyl group, an ethyl group and a trifluoromethyl group; and preferable examples of the alkoxy group include a C_1 - C_5 alkoxy group which may be branched such as a methoxy group and an ethoxy group. Examples of the halogen atom of the alkyl group which may be substituted by a halogen atom include a fluorine atom, a chlorine atom, and a bromine atom. Examples of the lower alkyl group represented by R^4 or R^5 include a methyl group, an ethyl group, a propyl group, and an isopropyl group. Preferable examples of the alkoxy group represented by R^6 include a C_1 - C_5 alkoxy group which may be branched such as a methoxy group and an ethoxy group; and preferable examples of the alkyl group include a C_1 - C_3 alkyl group which may be branched such as a methyl group, an ethyl group, and a propyl group.

[0031] Preferable examples of the integer shown by n include 1, 2, and 3.

[0032] In the general formula (If):

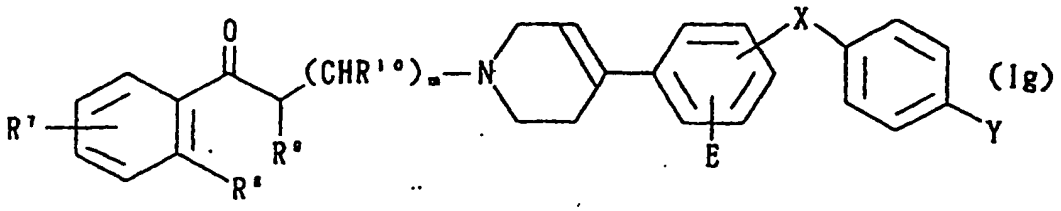


wherein E, R^3, R^4, R^5, R^6, X, Y, and n are as defined above, preferable examples of the halogen atom represented by R^3 include a fluorine atom, a chlorine atom and a bromine atom; preferable examples of the alkyl group which may be substituted by a halogen atom include a C_1 - C_5 alkyl group which may be branched such as a methyl group, an ethyl group and a trifluoromethyl group; and preferable examples of the alkoxy group include a C_1 - C_5 alkoxy group which may be branched such as a methoxy group and an ethoxy group. Examples of the halogen atom of the alkyl group which may be substituted by a halogen atom include a fluorine atom, a chlorine atom, and a bromine atom. Examples of the lower alkyl group represented by R^4 or R^5 include a methyl group, an ethyl group, a propyl group, and an isopropyl group. Preferable examples of the alkoxyl group represented by R^6 include a C_1 - C_5 alkoxyl group which may be branched such as a methoxy group and an ethoxy group; and preferable examples of the alkyl group include a C_1 - C_5 alkyl group which may be branched such as a methyl group, an ethyl group, and a propyl group.

[0033] Preferable examples of the integer shown by n include 1, 2, and 3.

[0034] The substitution of X for the benzene ring is in a para position.

[0035] In the general formula (Ig):

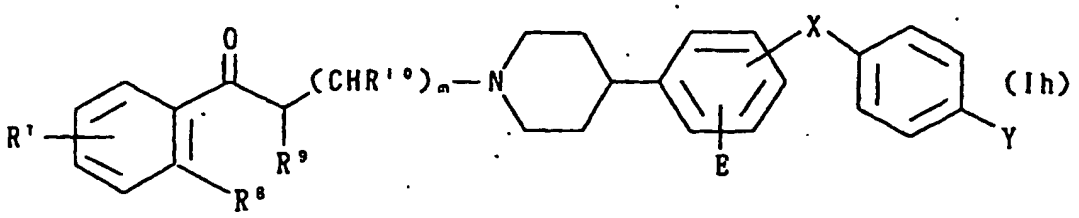


wherein R^7 represents a hydrogen atom, a halogen atom, an alkyl group which may be substituted by a halogen atom, an alkoxy group, or a hydroxyl group, R^8 and R^9 are the same or different from each other and represent a hydrogen atom, or an alkyl group, or R^8 and R^9 are taken together to represent a methylene group, R^{10} represents a hydrogen atom, a hydroxyl group, an alkoxy group or an alkyl group, m is an integer from 0 to 6, and E, X and Y are as defined above,

preferable examples of the halogen atom represented by R^7 include a fluorine atom, a chlorine atom, and a bromine atom; preferable examples of the alkyl group which may be substituted by a halogen atom include a C_1 - C_5 alkyl group which may be branched such as a methyl group, an ethyl group and a trifluoromethyl group; and preferable examples of the alkoxy group include a C_1 - C_5 alkoxy group which may be branched such as a methoxy group, and an ethoxy group. Examples of the halogen atom of the alkyl group which may be substituted by a halogen atom include a fluorine atom, a chlorine atom, and a bromine atom. Preferable examples of the alkyl group represented by R^8 or R^9 include a C_1 - C_5 alkyl group which may be branched such as a methyl group, an ethyl group, and a propyl group. Preferable examples of the alkoxy group represented by R^{10} include a C_1 - C_5 alkoxy group which may be branched such as a methoxy group and an ethoxy group; and preferable examples of the alkyl group include a C_1 - C_5 alkyl group which may be branched such as a methyl group, an ethyl group, and a propyl group.

[0036] Preferable examples of the integer of 0 to 6 shown by m include 0, 1, 2, 3, and 4.

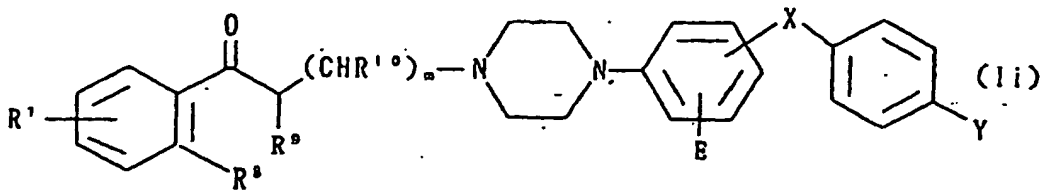
[0037] In the general formula (Ih):



wherein E, R^7, R^8, R^9, R^{10}, X, Y and m are as defined above, preferable examples of the halogen atom represented by R^7 include a fluorine atom, a chlorine atom, and a bromine atom; preferable examples of the alkyl group which may be substituted by a halogen atom include a C_1 - C_5 alkyl group which may be branched such as a methyl group, an ethyl group and a trifluoromethyl group; and preferable examples of the alkoxy group include a C_1 - C_5 alkoxy group which may be branched such as a methoxy group, and an ethoxy group. Examples of the halogen atom of the alkyl group which may be substituted by a halogen atom include a fluorine atom, a chlorine atom, and a bromine atom. Preferable examples of the alkyl group represented by R^8 or R^9 include a C_1 - C_5 alkyl group which may be branched such as a methyl group, an ethyl group, and a propyl group. Preferable examples of the alkoxy group represented by R^{10} include a C_1 - C_5 alkoxy group which may be branched such as a methoxy group and an ethoxy group; and preferable examples of the alkyl group include a C_1 - C_5 alkyl group which may be branched such as a methyl group, an ethyl group, and a propyl group.

[0038] Preferable examples of the integer of 0 to 6 shown by m include 0, 1, 2, 3, and 4.

[0039] In the general formula (Ii):

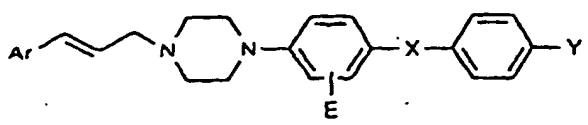


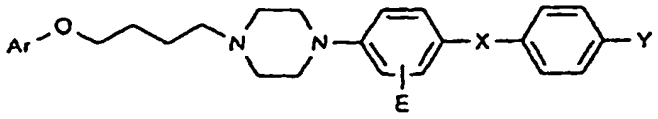
wherein E, R^7, R^8, R^9, R^{10}, X, Y and m are as defined above, preferable examples of the halogen atom represented by R^7 include a fluorine atom, a chlorine atom, and a bromine atom; preferable examples of the alkyl group which may be substituted by a halogen atom include a C_1 - C_5 alkyl group which may be branched such as a methyl group, an ethyl group and a trifluoromethyl group; and preferable examples of the alkoxyl group include a C_1 - C_5 alkoxy group which may be branched such as a methoxy group, and an ethoxy group. Examples of the halogen atom of the alkyl group which may be substituted by a halogen atom include a fluorine atom, a chlorine atom, and a bromine atom. Preferable examples of the alkyl group represented by R^8 or R^9 include a C_1 - C_5 alkyl group which may be branched such as a methyl group, an ethyl group, and a propyl group. Preferable examples of the alkoxy group represented by R^{10} include a C_1 - C_5 alkoxy group which may be branched such as a methoxy group and an ethoxy group; and preferable examples of the alkyl group include a C_1 - C_5 alkyl group which may be branched such as a methyl group, an ethyl group, and a propyl group.

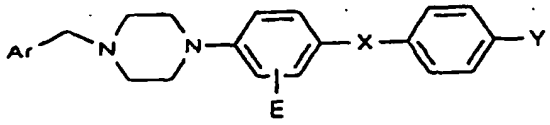
[0040] Preferable examples of the integer of 0 to 6 shown by m include 0, 1, 2, 3, and 4.

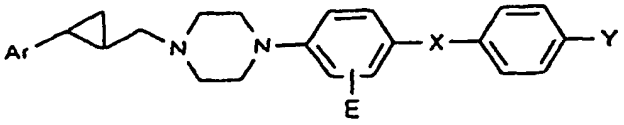
[0041] The substitution of X for the benzene ring is in a para position.

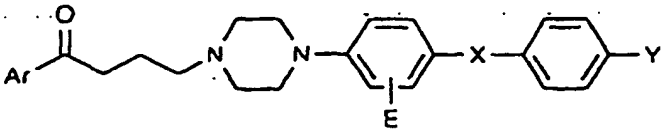
[0042] Among the compounds represented by the general formula (I), particularly preferable compounds are as follows:

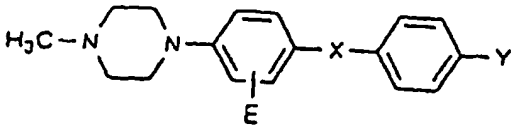


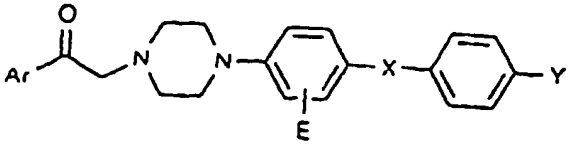


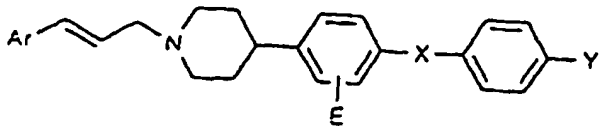


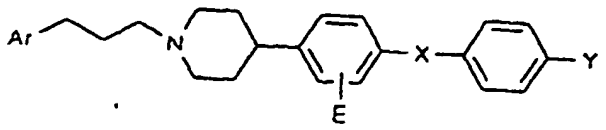


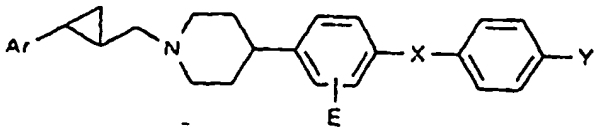


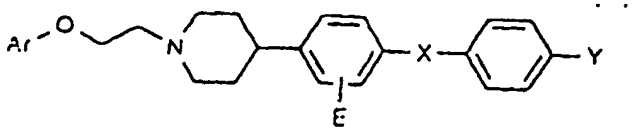


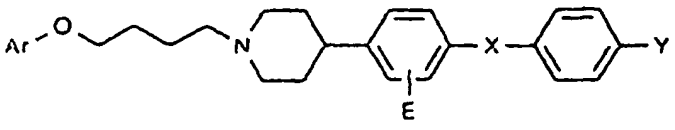


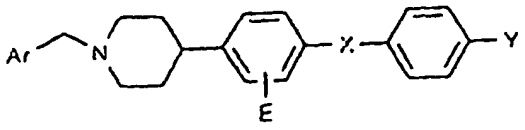


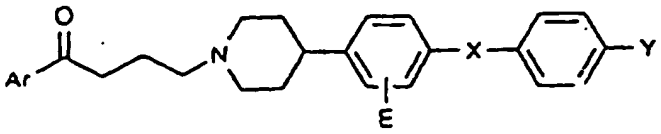


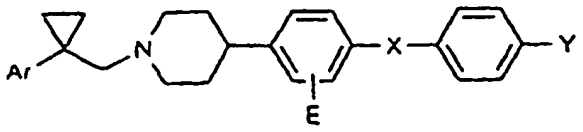


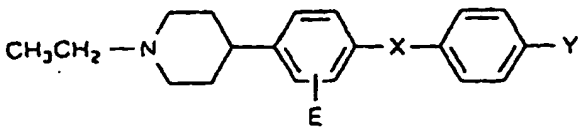


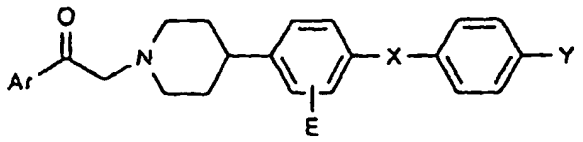


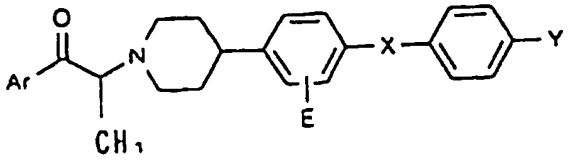


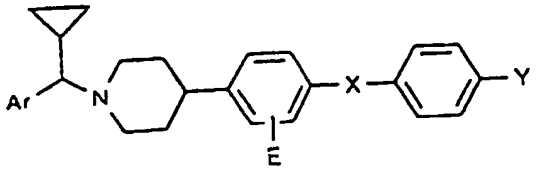


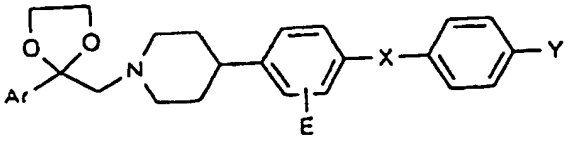


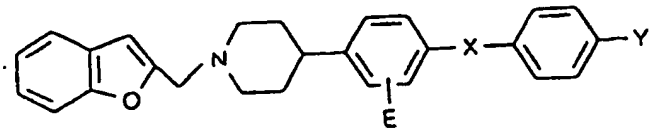


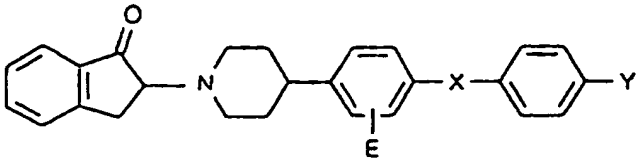


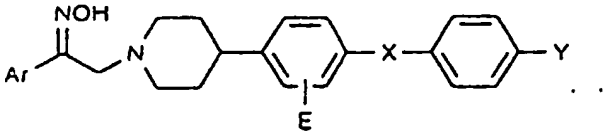


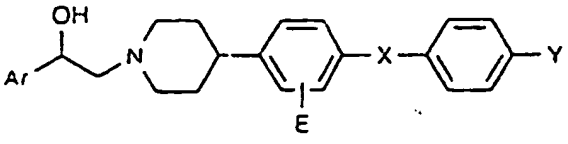


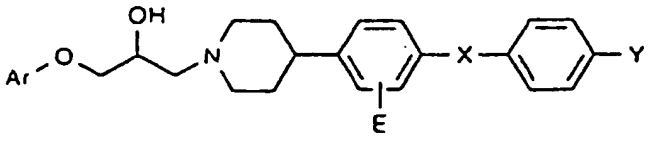


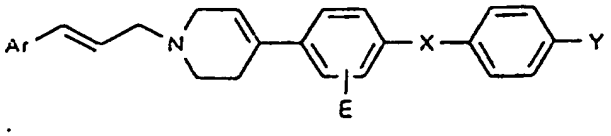


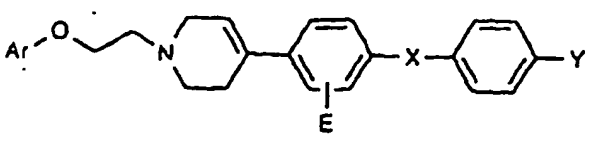






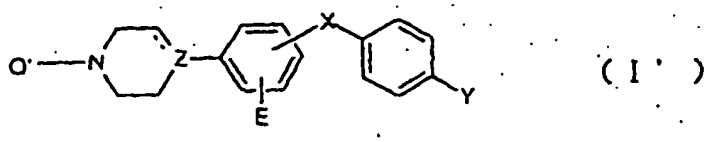






wherein, Ar represents a phenyl group and E, X, and Y are as defined above.

[0043] Further, the present invention provides compounds having the general formula (I') and their salts:



(I')

wherein, Q' represents a group having the formula:

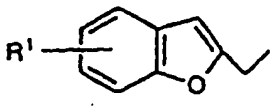
R'-A-B-

in which R' represents a substituted or unsubstituted phenyl group, a substituted or unsubsituted phenoxy group, or substituted or unsubstituted benzoyl group,

A represents a connecting bond, a cycloalkylene group, an alkenylene group which may be substituted by a lower alkyl group, a dialkoxymethylene group, or a hydroxyiminomethylene group, and

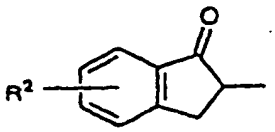
B represents an alkylene group which may be substituted by a hydroxy group or an alkoxy group;

a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, an alkyl group which may be substituted by a halogen atom, an alkoxy group, or a hydroxyl group; or

a group having the formula:



in which R^2 represents a hydrogen atom, a halogen atom, an alkyl group which may be substituted by a halogen atom, an alkoxy group, or a hydroxyl group,

X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring is in a para position,

E and Y may be the same or different from each oher and represent a hydrogen atom, a hydroxyl group, a halogen atom, an alkoxy group, or an alkyl group which may be substituted by a halogen atom,

the dotted line shows the presence or absence of a bond, when said dotted line shows the presence of a bond, Z represents a carbon atom, when said dotted line shows the absence of a bond, Z represents CH or a nitrogen atom,

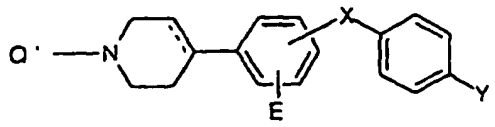
when Z is a carbon atom or CH, X is a methylene group, A is a connecting bond, and B is an unsubstituted alkylene group, R' does not represent an unsubstituted phenyl group.

[0044] Preferable examples of substituent for the substituted or unsubstituted phenyl group, substituted or unsubstituted phenoxy group or substituted or unsubstituted benzoyl group represented by R' include a halogen atom such as a fluorine atom, a chlorine atom, and a bromine atom, a hydroxyl group, a C_1 - C_5 alkoxy group which may be branched such as a methoxy group and an ethoxy group, a C_1 - C_5 alkyl group which may be branched and may be substituted by a halogen atom such as a methyl group, an ethyl group and a trifluoromethyl group. Examples of the halogen atom of the C_1 - C_5 alkyl group which may be branched and may be substituted by a halogen atom include a fluorine atom, a chlorine atom, and a bromine atom.

[0045] The preferable examples of the cycloalkylene group, the alkenylene group which may be substituted by a lower alkyl group, or the dialkoxymethylene group represented by A, preferable examples of the alkylene group which

may be substituted by a hydroxyl group or an alkoxy group represented by B, preferable examples of the halogen atom, the alkoxy group, or the alkyl group which may be substituted by a halogen atom represented by E or Y, and preferable examples of the halogen atom, the alkyl group which may be substituted by a halogen atom, and the alkoxy group represented by R^1 or R^7 are the same as with A, B, E, Y, R^1 and R^2 in the above general formula (I).

[0046] The present invention further provides compounds having the general formula (I'') and their salts:



(I'')

wherein, Q' represents a group having the formula:

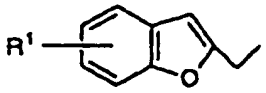
R'-A-B-

in which R' represents a substitued or unsubstituted phenyl group, substituted or unsubstituted phenoxy group, or substituted or unsubstituted benzoyl group,

A represents a connecting bond, a cycloalkylene group, an alkenylene group which may be substituted by a lower alkyl group, a dialkoxymethylene group, or a hydroxyiminomethylene group, and

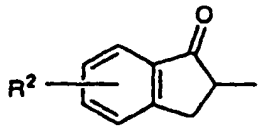
B represents a hydroxyl group- or alkoxyl group-an alkylene group which may be substituted by a hydroxyl group or an alkoxy group;

a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, an alkyl group which may be substituted by a halogen atom, an alkoxy group, or a hydroxyl group; or

a group having the formula:



in which R^2 represents a hydrogen atom, a halogen atom, an alkyl group which may be substituted by a halogen atom, an alkoxy group, or a hydroxyl group,

X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring is in a para position,

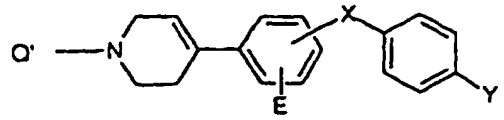
E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, an alkoxy group, or an alkyl group which may be substituted by a halogen atom,

the dotted line shows the presence or absence of a bond, and when X is a methylene group, A is a connecting bond and B is an unsubstituted alkylene group, R' does not represent an unsubstituted phenyl group.

[0047] The preferable examples of the substituent of the substituted or unsubstituted phenyl group, substituted or unsubstituted phenoxy group, or substituted or unsubstituted benzoyl group represented by R', preferable examples of the cycloalkylene group, the alkenylene group which may be substituted by a lower alkyl group or the dialkoxymethylene group represented by A, preferable examples of the alkylene group which may be substituted by a hydroxyl group or an alkoxy group represented by B, preferable examples of the halogen atom, the alkoxy group, or the alkyl group which may be substituted by a halogen atom represented by E or Y, and preferable examples of the halogen atom, the alkyl group which may be substituted by a halogen atom, and the alkoxyl group represented by R^1 or R^2 are the same as with R', A, B, E, Y, R^1 and R^2 in the above general formula (I').

[0048] The compounds having the general formula (I") include the compounds having the general formulas (I"a) and (I"b).

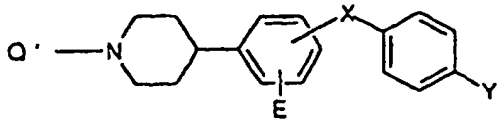
[0049] In the general formula (I"a):



(I"a)

wherein, Q', E, X, and Y are as defined above.

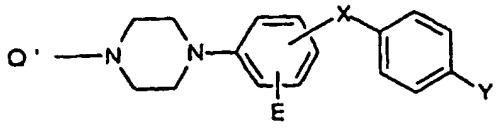
[0050] In the general formula (I"b):



(I"b)

wherein, Q', E, X, and Y are as defined above.

[0051] The present invention further provides compounds having the general formula (I'") and their salts:



(I'")

wherein, Q' represents a group having the formula:

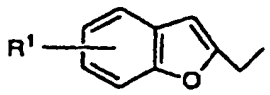
R'-A-B-

in which R' represents a substituted or unsubstituted phenyl group, substituted or unsubstituted phenoxy group, or substituted or unsubstituted benzoyl group,

A represents a connecting bond, a cycloalkylene group, an alkenylene group which may be substituted by a lower alkyl group, a dialkoxymethylene group, or a hydroxyiminomethylene group, and

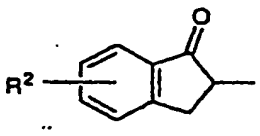
B represents an alkylene group which may be substituted by a hydroxy group or an alkoxy group;

a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, an alkyl group which may be substituted by a halogen atom, an alkoxyl group, or a hydroxyl group; or

a group having the formula:



in which R^2 represents a hydrogen atom, a halogen atom, an alkyl group which may be substituted by a halogen atom, an alkoxy group, or a hydroxyl group,

X represents an oxygen atom or methylene group, the substitution of X for the benzene ring is in a para position, and

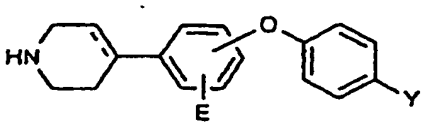
E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, an alkoxy group, or an alkyl group which may be substituted by a halogen atom.

[0052] The examples of the preferable substituent for the substituted or unsubstituted phenyl group, substituted or unsubstituted phenoxy group, or substituted or unsubstituted benzoyl group represented by R', preferable examples of the cycloalkylene group, the alkenylene group which may be substituted by a lower alkyl group, or the dialkoxymethylene group represented by A, preferable examples of the alkylene group which may be substituted by a hydroxyl group or alkoxy group represented by B, preferable examples of the halogen atom, the alkoxy group, or the alkyl group which may be substituted by a halogen atom represented by E or Y and preferable examples of the halogen atom, the alkyl group which may be substituted by a halogen atom, or an alkoxy group represented by R^1 or R^2 are the same as with R', A, B, E, Y, R^1 and R^2 in the above general formula (I').

[0053] The compounds having the general formulas (I), (I'), (I''), and (I''') of the present invention include isomers. The present invention includes all of these isomers and mixtures of the same. For example, in the general formulas (I), (I'), (I'') and (I'''), when B represents an alkylene group which may be substituted by a hydroxyl group or an alkoxyl group, there are two optical isomers, when A represents a hydroxyiminomethylene group and an alkenylene group which may be substituted by a lower alkyl group, there are two geometric isomers, (E)-form and (Z)-form. The compounds of the present invention include the individual isomers and all mixtures of combinations of the same.

[0054] According to the present invention, further, there are provided compounds of the general formula (IIa):

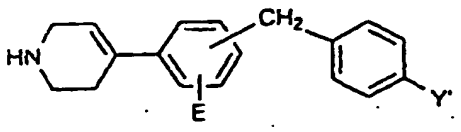
[0055] General formula (IIa):



(IIa)

wherein, E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, an alkoxy group, or an alkyl group which may be substituted by a halogen atom, the dotted line shows the presence or absence of a bond, and the substitution of the benzene ring bonding with the piperidine ring or tetrahydropyridine ring and the group $-OC_6H_4Y$ is in a para position.

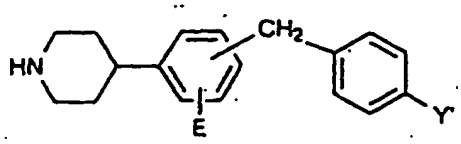
[0056] According to the present invention, further, there are provided compounds having the general formula (IIb):



(IIb)

wherein, E represents a hydrogen atom, hydroxyl group, a halogen atom, an alkoxy group, or an alkyl group which may be substituted by a halogen atom, Y' represents a hydroxyl group, a halogen atom, an alkoxy group, or an alkyl group which may be substituted by a halogen atom, and the substitution of the benzene ring bonding with the tetrahydropyridine ring and group $-CH_2C_6H_4Y'$ is in a para position.

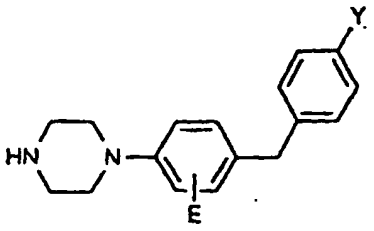
[0057] According to the present invention, further, there are provided compounds having the general formula (IIc):



(IIc)

wherein, E represents a hydrogen atom, a hydroxyl group, a halogen atom, an alkoxyl group, or an alkyl group which may be substituted by a halogen atom, Y' represents a hydroxyl group, a halogen atom, alkoxyl group, or an alkyl group which may be substituted by a halogen atom, and the substitution of the benzene ring bonding with the piperidine ring and the group $-CH_2C_6H_4Y'$ is in a para position.

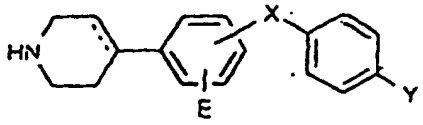
[0058] According to the present invention, further, there are provided compounds having the general formula (IIIa):



(IIIa)

wherein, E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, an alkoxy group, or an alkyl group which may be substituted by a halogen atom.

[0059] The compounds (Ia), (Id), (Ig) and (I"a) in the general formulas (I), (I'), and (I") wherein Z represents a carbon atom and the compounds (Ib), (Ie), (Ih) and (I"b) wherein Z represents CH may be synthesized from compounds having the general formula (II):

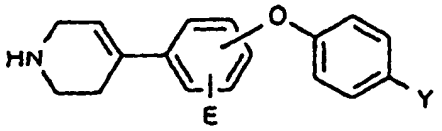


(II)

wherein, E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, an alkoxy group, or an alkyl group which may be substituted by a halogen atom, and the dotted line shows the presence or absence of a bond.

[0060] The compounds (II) are explained by the general formulas (IId), (IIe), (IIf) and (IIg).

[0061] In the general formula (IId):

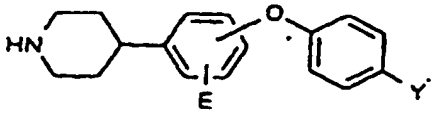


(IId)

wherein, E and Y are as defined above,

preferable examples of the halogen atom represented by E or Y include a fluorine atom, a chlorine atom, and a bromine atom; preferable examples of the alkoxy group include a C_1 - C_5 alkoxy group which may be branched such as a methoxy group, and an ethoxy group; and preferable examples of the alkyl group which may be substituted by a halogen atom include a C_1 - C_5 alkyl group which may be branched such as a methyl group, an ethyl group, and a trifluoromethyl group. Examples of the halogen atom of the alkyl group which may be substituted by a halogen atom include a fluorine atom, a chlorine atom, and a bromine atom. The substitution of the benzene ring bonding with the tetrahydropyridine ring and the group $-OC_6H_4Y$ is in a para position.

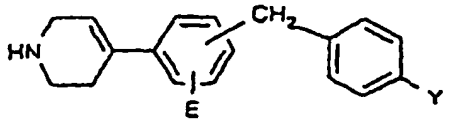
[0062] In the general formula (IIe):



(IIe)

wherein E and Y are as defined above,
preferable examples of the halogen atom represented by E or Y include a fluorine atom, a chlorine atom, and a bromine atom; preferable examples of the alkoxy group include a C_1 - C_5 alkoxy group which may be branched such as a methoxy group, and an ethoxy group; and preferable examples of the alkyl group which may be substituted by a halogen atom include a C_1 - C_5 alkyl group which may be branched such as a methyl group, an ethyl group, and a trifluoromethyl group. Examples of the halogen atom of the alkyl group which may be substituted by a halogen atom include a fluorine atom, a chlorine atom, and a bromine atom. The substitution of the benzene ring bonding with the piperidine ring and the group $-OC_6H_4Y$ is in a para position.

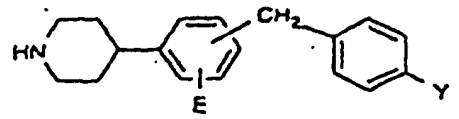
[0063] In the general formula (IIf):



(IIf)

wherein E and Y are as defined above,
preferable examples of the halogen atom represented by E or Y include a fluorine atom, a chlorine atom, and a bromine atom; preferable examples of the alkoxy group include a C_1 - C_5 alkoxy group which may be branched such as a methoxy group, and an ethoxy group; and preferable examples of the alkyl group which may be substituted by a halogen atom include a C_1 - C_5 alkyl group which may be branched such as a methyl group, an ethyl group, and a trifluoromethyl group. Examples of the halogen atom of the alkyl group which may be substituted by a halogen atom include a fluorine atom, a chlorine atom, and a bromine atom. The substitution of the benzene ring bonding with the tetrahydropyridine ring and the group $-CH_2C_6H_4Y$ is in a para position.

[0064] In the general formula (IIg):



(IIg)

wherein, E and Y are as defined above,
preferable examples of the halogen atom represented by E or Y include a fluorine atom, a chlorine atom, and a bromine atom; preferable examples of the alkoxy group include a C_1 - C_5 alkoxy group which may be branched such as a methoxy group, and an ethoxy group; and preferable examples of the alkyl group which may be substituted by a halogen atom include a C_1 - C_5 alkyl group which may be branched such as a methyl group, an ethyl group, and a trifluoromethyl group. Examples of the halogen atom of the alkyl group which may be substituted by a halogen atom include a fluorine atom, a chlorine atom, and a bromine atom. The substitution of the benzene ring bonding with the piperidine ring and the group $-CH_2C_6H_4Y$ is in a para position.

[0065] The compounds of the general formulas (I), (I'), (I") or (I'"), for example, may be synthesized in the following manners. These methods will be successively explained below.

[0066] The compounds (Ia), (Id), (Ig), and (I"a), (If) of the general formulas (I), (I'), and (I") wherein Z represents a carbon atom and the compounds (Ib), (Ie), (Ih), and (I"b), (Ig) wherein Z represents CH can be obtained as follows:

[0067] The compound (IIh) is obtained from a known starting material (IV) (step 1), then the compound (IIi) is obtained from the compound (IIh) (step 2). The compounds (Ia), (Id), (Ig), or (I"a) can be obtained from the compound (IIh) (step 3) and the compound (Ib), (Ie), (Ih), or (I"b) can be obtained from the compound (IIi) (step 4).

[0068] For compounds having the general formulas (I), (I'), and (I") wherein A represents an alkenylene group, the compound (Ij) can be obtained from the compound (IIh) (step 5) and the compound (Ik) can be obtained from the compound (IIi) (step 6).

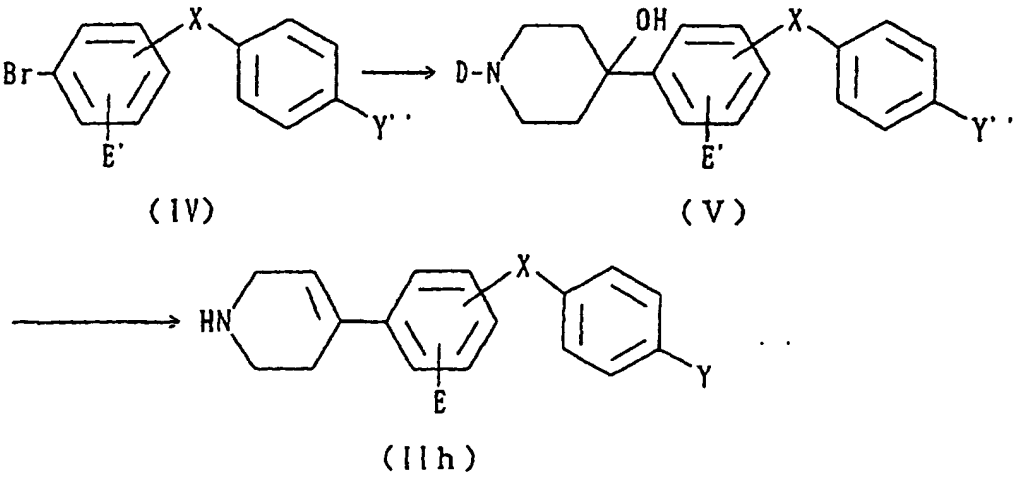
[0069] For compounds having the general formulas (I), (I'), and (I") wherein B represents a hydroxyl group-substituted alkylene group, the compound (II) can be obtained from the compound (IIh) (step 7) and the compound (Im) can be obtained from the compound (IIi) (step 8).

[0070] For compounds having the general formulas (I), (I'), and (I") wherein B represents a methylene group, the compound (In) can be obtained from the compound (IIh) (step 9) and the compound (Io) can be obtained from the compound (IIi) (step 10).

[0071] Further, the compounds (Ic), (If), or (Ii) having the general formula (I) wherein Z represents a nitrogen atom or the compound (I"') having the general formula (I') wherein Z represents a nitrogen atom can be obtained from the known starting material (X) (step 11).

Step 1:

[0072] The compound (IIh) can be synthesized in accordance with the following method from the known starting material (IV):



wherein, E, X, and Y are as defined above, E' and Y" may be the same or different and represent a hydrogen atom, a halogen atom, alkoxyl group, or a halogen atom-substitutable alkyl group, and D represents a tert-butoxycarbonyl group, ethoxycarbonyl group, or acetyl group.

[0073] That is, the aryl bromide derivative having the general formula (IV) is converted by the conventional method to the corresponding aryl Grignard reagent or aryl lithium reagent, then is allowed to react in tetrahydrofuran, diethylether, ethyleneglycol dimethylether, toluene, or another solvent not participating in the reaction, at -100 to 50°C, preferably -78°C to room temperature, with 1 to 1.5 equivalents of the known starting material N-tert-butoxycarbonyl-4-piperidone, N-ethoxy carbonyl-4-piperidone, or N-acetyl-4-piperidone for 1 to 6 hours so as to obtain the compound having the general formula (V).

[0074] The starting substance (IV) used in the reaction is a known compound as described in Martin et al. [L. Martin et al: J. Med. Chem., 22, 1347 (1979)] or can be synthesized by the similar method. For example, 4-bromodiphenylether, 4- bromodiphenylmethane, 4-bromo-4'-fluorodiphenylmethane, 4-bromo-4'-chlorodiphenylmethane, 4-bromo-4'-methoxydiphenylmethane, 4-bromo-4'-trifluoromethyldiphenylmethane, and the like may be used. Further, as the conditions for preparing the Grignard reagent and the organolithium reagent, use may be made of the various methods described in the "Compendium for Organic Synthesis" (Wiley-Interscience: A Division of John Wiley & Sons Ltd.) etc.

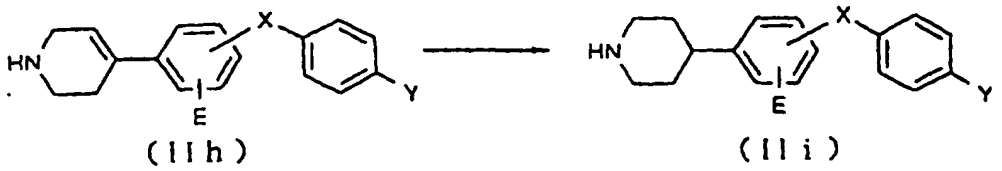
[0075] The compound obtained from the reaction can be used as is for the next step or if necessary can be used after purification by a generally used purification method such as recrystallization or column chromatography.

[0076] Next, the compound (V) thus obtained is treated under non-solvent conditions or in tetrahydrofuran, diethyl ether, ethyleneglycol dimethylether, benzene, toluene, methylene chloride, chloroform, carbon tetrachloride, water, methanol, ethanol, or another solvent not participating in the reaction, at -20 to 150°C, preferably 0 to 80°C, with 1 to 20 equivalents of organic acids such as acetic acid, trifluoroacetic acid, methanesulfonic acid, trifluoromethanesulfonic acid, and the like or inorganic acids such as hydrochloric acid, sulfuric acid, nitric acid, and the like for 1 to 12 hours, or the compound (V) is let to react in benzene, toluene, methylene chloride, chloroform, carbon tetrachloride, or another

solvent not participating in the reaction, if necessary in the presence of triethylamine, pyridine, diisopropylethylamine, or other bases, at -20 to 150°C, preferably 0 to 100°C, with 1 to 5 equivalents of thionylchloride, methane sulfonylchloride, trifluoromethane sulfonylchloride, trifluoromethanesulfonic acid anhydride, p-toluene sulfonylchloride, phosphorus oxychloride, or other acid chloride derivatives for 1 to 6 hours, then performing an acid treatment similar to the above, so as to obtain a compound having the general formula (IIh). Further, compounds having the general formula (IIh) wherein E or Y represents a hydroxyl group can be obtained by dealkylating a compound having the general formula (IIh) wherein E or Y represents an alkoxy group using the various methods described in "Protective Groups in Organic Synthesis" (T. W. Greene, John Wiley & Sons Ltd.) etc.

Step 2:

[0077] The compound (IIh) obtained in step 1 can be reduced to synthesize the compound (IIi):



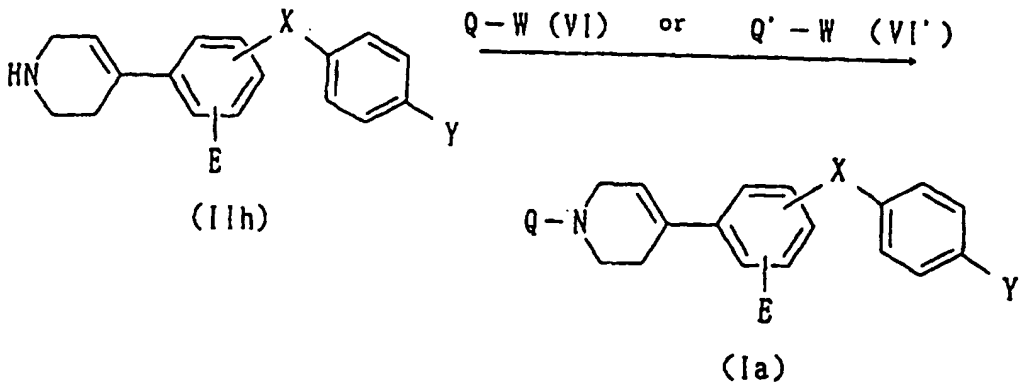
(IIh) (IIi)

(wherein, E, X, and Y are as defined above.)

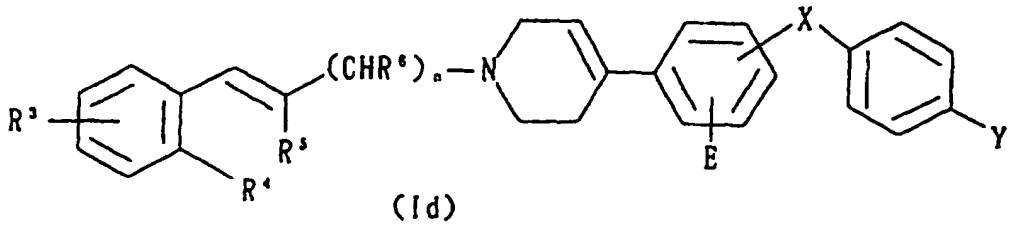
[0078] That is, the compound (IIh) obtained in step 1 can be hydrogenated in the presence of palladium carbon, platinum, or another catalyst in methanol, ethanol, ethyl acetate, or another solvent not participating in the reaction at room temperature so as to convert it to the compound having the general formula (IIi). Further, in the present reaction, if necessary, acetic acid, hydrochloric acid, or another acid may be added.

Step 3:

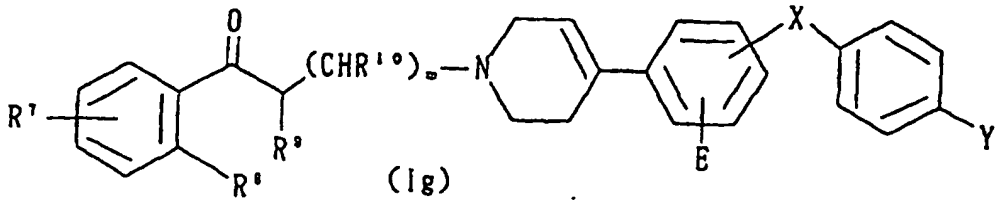
[0079] The compound (IIh) obtained in step 1 can be reacted with the compound (VI) or (VI') to synthesize the compounds (Ia), (Id), (Ig), or (I"a) having the general formula (I), (I') and (I") wherein Z is a carbon atom.



(IIh) (Ia)

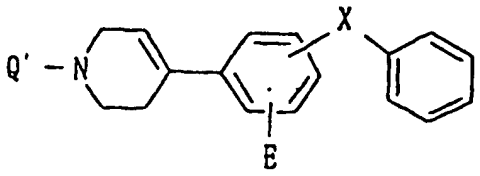


(Id)



(Ig)

or



(I''a)

(wherein, Q, Q', E, X, Y, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, m, and n are as defined above, and W represents a group able to be easily exchanged with an amine group).

[0080] That is, the compound (IIh) obtained in step 1 may be allowed to react in tetrahydrofuran, diethylether, ethyleneglycol dimethylether, dioxane, acetonitrile, benzene, toluene, dimethylformamide, dimethylsulfoxide, or another solvent not participating in the reaction, in the presence of triethylamine, diisopropylethylamine, pyridine, or another organic base or sodium, potassium, sodium hydride, potassium hydride, sodium amide, sodium ethoxide, potassium tert-butoxide, sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, cesium fluoride, or other inorganic bases, at -20 to 150°C, preferably room temperature to 100°C, with 1 to 1.5 equivalents of the compound (VI) or (VI') for 1 to 24 hours so as to obtain the tetrahydropyridine derivative of the general formula (Ia), (Id), (Ig), or (I"a). Further, in the present reaction, if necessary, sodium iodide or tetrabutylammonium iodide may be added.

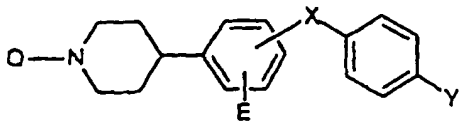
[0081] W is a leaving group capable of being easily exchanged with an amine group and for example is a chlorine atom, bromine atom, or other halogen atom, alkylsulfonyloxy group such as a methane sulfonyloxy group or arylsulfonyloxy group such as a p-toluene sulfonyloxy group.

[0082] As the compound (VI) or (VI') usable in the present reaction, a commercially available or known compound may be used, for example, methyl iodide, ethyl iodide, ethyl bromide, propyl bromide, cinnamyl bromide, 3-bromo-2-methyl-1-phenyl-1-propene, 4-fluorocinnamyl bromide, (2,3,4-trimethoxy)cinnamyl bromide, 1-bromo-3-phenylpropane, (1-bromoethyl)benzene, (2-bromoethyl)benzene, 4-methoxycinnamyl bromide, 2-(4-fluorophenyl)oxyethyl bromide, 2-phenyloxyethyl bromide, 4-(4-fluorophenyl)oxybutyl bromide, 4-phenyloxybutyl bromide, 2-phenyloxypropyl bromide, trans-(2-phenyl) cyclopropylmethyl bromide, 1-phenyl-1-cyclopropylmethyl bromide, 1-phenyl-1-cyclopropanemethyl bromide, 1-phenyl-1-cyclopentanemethyl bromide, phenacyl bromide, 2-bromo-4'-methoxyacetophenone, 2-bromo-4'-fluoroacetophenone, 2-bromo-4'-chloroacetophenone, 2-bromopropiophenone, 2-bromo-2',4'-dimethoxyacetophenone, 2-bromo-2',5'-dimethoxyacetophenone, 2-bromo-4'-methylacetophenon, 4-chlorobutyrophenone, 4-chloro-4'-fluorobutyrophenone, 2-bromomethyl-2-phenyl-1,3-dioxolane, 2-bromomethyl-2-(4-fluorophenyl)-1,3-dioxolane, 2-bromomethyl-2-(4-chlorophenyl)-1,3-dioxolane, 2-bromomethyl-2-(4-methoxyphenyl)-1,3-dioxolane, 2-(1-bromoethyl)-2-phenyl-1,3-dioxolane, 2-bromomethyl-2-(4-methylphenyl)-1,3-dioxolane, 2-bromomethyl-2-(2,4-dimethoxyphenyl)-1,3-dioxolane, 2-bromomethyl-2-(2,5-dimethoxyphenyl)-1,3-d ioxolane, 2,3,4-trimethoxybenzylchloride, benzyl bromide, 4-fluorobenzyl bromide, 2-fluorobenzyl bromide, 3-fluorobenzyl bromide, 4-(trifluoromethyl)benzyl bromide, 2-(trifluoromethyl)benzyl bromide, 3-(trifluoromethyl) benzyl bromide, 2-bromo-1-indanone, 2-bromomethyl-benzofuran, (2-bromo-1-hydroxyiminoethyl)benzene, 3-methoxybenzyl chloride, 4-methoxybenzyl chloride, cinnamyl chloride, (2-bromo-1-methoxyethyl)benzene, 1-(4-chlorophenyl)cyclobutanemethyl bromide, 1-(4-chlorophenyl)cyclopentanemethyl bromide, 1-(4-methoxyphenyl) cyclopentanemethyl bromide, (2-bromo-1,1-diethoxy ethyl) benzene, etc. may be used.

[0083] Further, the compounds of the general formulas (Ia) and (I"a) where A is a hydroxyiminomethylene group may be obtained by causing the corresponding ketone obtained in this step to react in pyridine, water, alcohol, water/alcohol or other solvent in the presence of pyridine, sodium hydroxide, potassium hydroxide, sodium hydrogencarbonate, potassium hydrogencarbonate, sodium carbonate, potassium carbonate or other base with hydroxyamine or its acid addition salt. Further, the compounds of the general formulas (Ia) and (I"a) where B is a hydroxyl group-substituted alkylene group may be obtained by reducing the corresponding ketone obtained in this step by sodium borohydride, lithium aluminum hydride, aluminum dibutyl hydride, borane, and other metal reducing agents or by catalyzing hydrogenation in the presence of a catalytic amount of palladium carbon, platinum, etc.

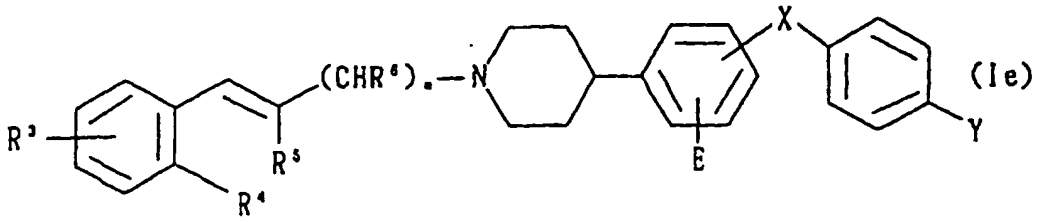
Step 4:

[0084] The compound (VI) can be reacted with the compound (IIi) obtained in step 2 by a similar method as in step 3 to synthesize the compound (Ib):



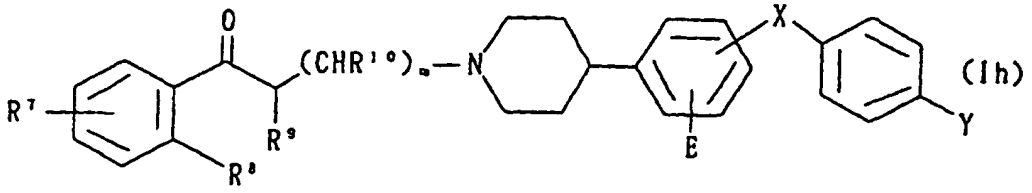
(Ib)

Compound (Ie):



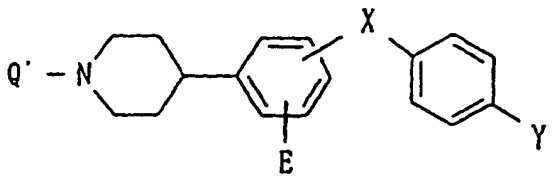
(Ie)

Compound (Ih):



(Ih)

or Compound (I"b):

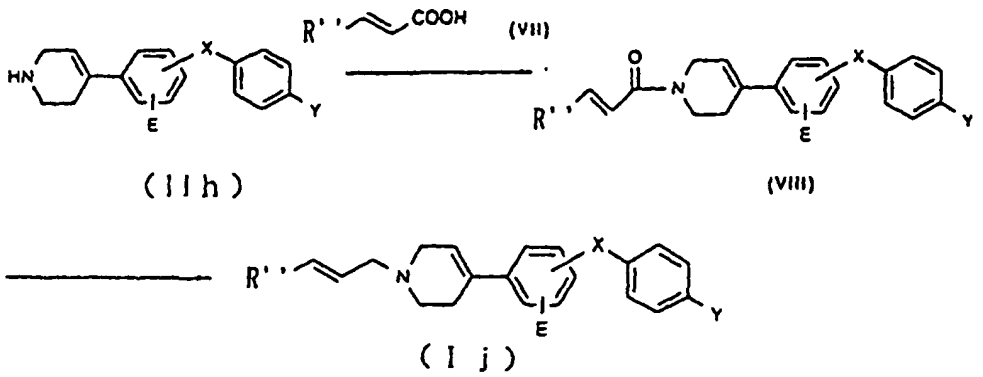


(I''b)

(wherein, Q', E, X, Y, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, n, and m are as defined above) having the general formula (I), (I'), and (I") where Z is CH.

Step 5:

[0085] The compounds (Ij) having the general formulas (I), (I'), and (I") wherein A is an alkenylene group and Z is a carbon atom can be synthesized from the compound (IIh) obtained in step 1:



(wherein, E, X, and Y are as defined above, and R" represents a substituted or unsubstituted phenyl group.)

[0086] That is, the compound (IIh) obtained at step 1 and the cinnamic acid derivative (VII) may be condensed by an ordinary method to convert to the amide derivative of the general formula (VIII), then reduced in tetrahydrofuran, diethylether, ethyleneglycol dimethylether, or another solvent not participating in the reaction at -100°C to 80°C, preferably -78°C to room temperature, by 1 to 5 equivalents of lithium aluminum hydride or sodium bis(2-methoxyethoxy) aluminum hydride for 1 to 12 hours.

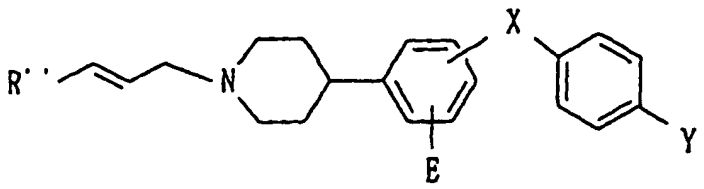
[0087] As the conditions of aforementioned amidation reaction, the various methods described in the "Compendium for Organic Synthesis" (Wiley-Interscience: A Division of John Wiley & Sons Ltd.)) etc. may be used. For example, the method of treating the cinnamic acid derivative (VII) if necessary in the presence of an organic or inorganic base with diethylphosphate cyanide (DEPC), diphenylphosphate adide (DPPA), dicyclohexylcarbodiimide (DCC), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, 2-iodo-1-methylpyridinium iodide, and the like may be used, or the cinnamic derivative (VII) may be made by an ordinary method into an acid halide, symmetric acid anhydride, mixed acid anhydride, or other active ester, etc., then condensed with the compound (IIh).

[0088] As the cinnamic acid derivative (VII) usable in the present reaction, a commercially available or known compound may be used, for example, cinnamic acid, 2,3,4-trimethoxycinnamic acid, α-methylcinnamic acid, 4-hydroxy-3-methoxycinnamic acid, 3-hydroxy-4-methoxycinnamic acid, 4-chlorocinnamic acid, 3-chlorocinnamic acid, 2-chlorocinnamic acid, 4-fluorocinnamic acid, 3-fluorocinnamic acid, 2-fluorocinnamic acid, 3,4,5-trimethoxycinnamic acid, 2-(trifluoromethyl)-cinnamic acid, 3-(trifluoromethyl)cinnamic acid, 4-(trifluoromethyl)cinnamic acid, 2-hydroxycinnamic acid, 3-hydroxycinnamic acid, 4-hydroxycinnamic acid, 2-methoxycinnamic acid, 3-methoxycinnamic acid, 4-methoxycinnamic acid, 2,6-difluorocinnamic acid, 2,4-difluorocinnamic acid, 2,5-difluorocinnamic acid, 3,4-difluorocinnamic acid, 3,5-difluorocinnamic acid, 2,6-dichlorocinnamic acid, 2,4-dichlorocinnamic acid, 3,4-dichlorocinnamic acid, 2,3-dimethoxycinnamic acid, 2,4-dimethoxycinnamic acid, 2,5-dimethoxycinnamic acid, 3,4-dimethoxycinnamic acid, 3,4-(methylenedioxy)cinnamic acid, 3,5-dimethoxycinnamic acid, 3,4-dihydroxycinnamic acid, 3,4-dimethoxy-4-hydroxycinnamic acid, 2,4,5-trimethoxycinnamic acid, α-methyl-2,4,5-trimethoxycinnamic acid, etc. may be used.

[0089] The compounds obtained in aforementioned reactions may be used as they are for the next step, but may also be used after purification if necessary by a generally used purification method such as recrystallization or column chromatography etc.

Step 6:

[0090] The compounds (Ik) having the general formulas (I), (I'), and (I") where A is an alkenylene group and Z is CH:

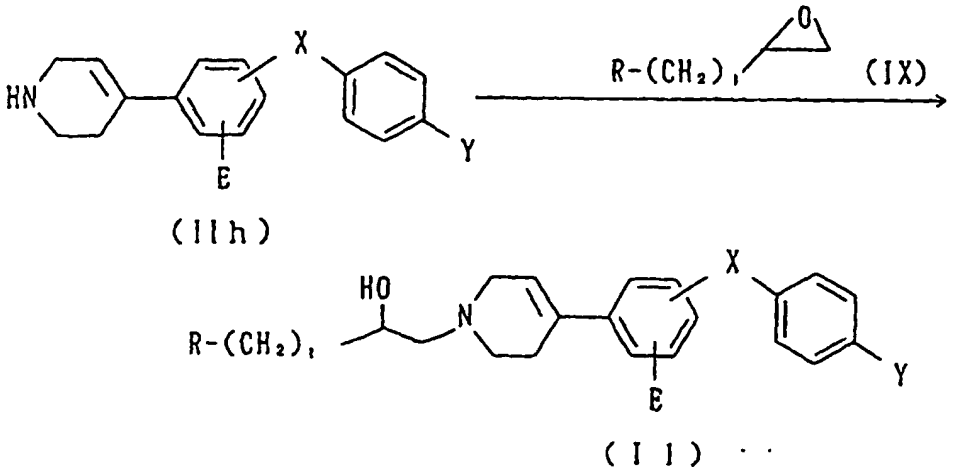


(I k)

wherein E, R", X, and Y are as defined above can be synthesized from the compound (IIi) obtained in step 2 by the similar method as step 5.

Step 7:

[0091] The compounds (II) having the general formulas (I), (I'), and (I") where A is a connecting bond, B is a hydroxyl group-substituted alkylene group, and Z is a carbon atom:



(IIh)

(I I)

(wherein, I represents an integer of 0 or 1, and E, R, X, and Y are as defined above),
can be synthesized from the compound (IIh) obtained at step 1.

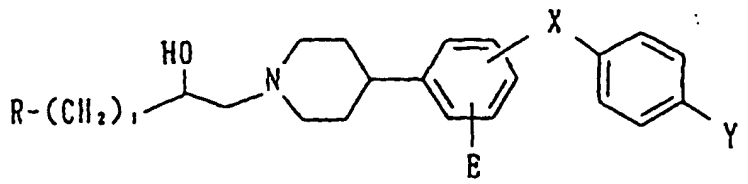
[0092] That is, compound (IIh) obtained at step 1 may be allowed to react in tetrahydrofuran, diethylether, ethyleneglycol dimethylether, dioxane, acetonitrile, benzene, toluene, dimethylformamide, dimethylsulfoxide, methanol, ethanol, isopropylalcohol, tert-butylalcohol, ethyleneglycol, or another solvent not participating in the reaction, at room temperature to 200°C, preferably 50°C to 150°C, with 0.9 to 1.5 equivalents of the compound (IX) for 1 to 24 hours.

[0093] As the compound (IX) usable in the present reaction, a commercially available or known compound may be used, for example, 1,2-epoxyethylbenzene, (R)-(+)-1,2-epoxyethylbenzene, (S)-(-)-1,2-epoxyethylbenzene, (1R,2R)-(+)-1-phenylpropylene oxide, (1S,2S)-(-)-1-phenylpropylene oxide, 1,2-epoxy-3-phenoxypropylene, (K)-(-)-2-(benzyloxymethyl)oxirane, (S)-(+)-2-(benzyloxymethyl)oxirane, 2,3-epoxypropylbenzene, glycidyl 2-methylphenyl ether, 4-tert-butylphenyl 2,3-epoxypropyl ether, 4-chlorophenyl 2,3-epoxypropyl ether, 2,3-epoxypropyl 4-methoxyphenyl ether, etc. may be used.

[0094] Further, in the present reaction, if necessary, triethylamine, diisopropylethylamine, pyridine and other organic bases, sodium, potassium, sodium hydroxide, potassium hydroxide, sodium amide, sodium ethoxide, potassium tert-butoxide, sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, cesium fluoride, and other inorganic bases, or sodium iodide, tetrabutylammonium iodide, lithium carbonate, lithium chloride, zinc bromide, magnesium bromide, and other metal salts may be added alone or in combinations of a plurality of types.

Step 8:

[0095] Using the same method as in step 7, the compounds (Im) of the general formulas (I), (I'), and (I") where A is a connecting bond, B is a hydroxyl group-substituted alkylene group, Z is CH:

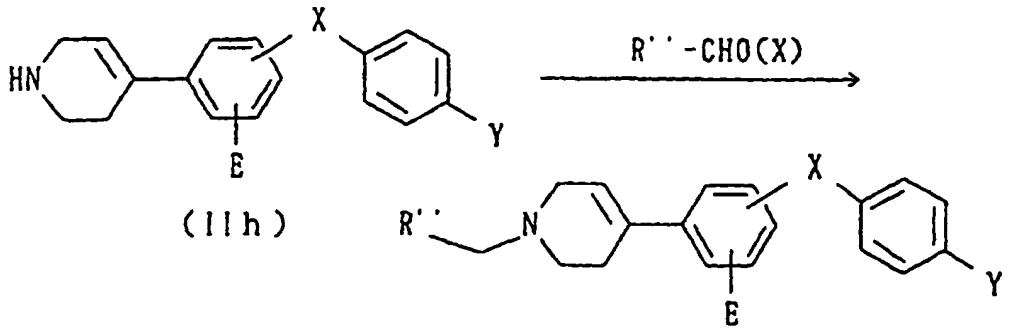


(I m)

(wherein, I, E, R, X, and Y are as defined above) can be synthesized from the compound (III) obtained at step 2.

Step 9:

[0096] The compounds (In) of the general formulas (I), (I'), and (I") wherein A is a connecting bond, B is a methylene group, and Z is a carbon atom can be synthesized from the compound (IIh) obtained in step 1.



(I n)

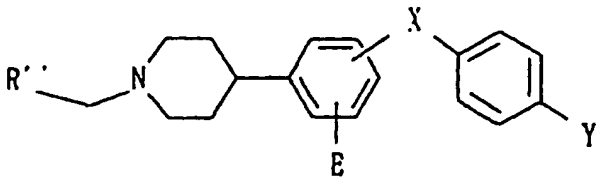
(wherein, E, R", X, and Y are as defined above.)

[0097] That is, the compound (IIh) obtained at step 1 and 1 to 1.2 equivalents of aldehyde (X) may be treated at room temperature to 200°C, preferably 80 to 150°C, while agitating, with 1 to 2 equivalents of formic acid to obtain the compound (In). Alternatively, the compound (IIh) and 1 to 1.2 equivalents of aldehyde may be treated in methanol, ethanol, isopropylalcohol, water, methanol/water or another solvent not participating in the reaction, if necessary adding sodium hydrogencarbonate, sodium dihydrogenphosphate, potassium dihydrogenphosphate, or aqueous solutions of the same, at -20 to 50°C, preferably 0°C to room temperature, by 0.3 to 2 equivalents of sodium cyanoborohydride to obtain the compound (In).

[0098] As the compound (X) usable in the present reaction, a commercially available or known compound may be used, for example, benzaldehyde, 2-fluorobenzaldehyde, 2-chlorobenzaldehyde, o-anisaldehyde, m-anisaldehyde, p-anisaldehyde, α,α,α-trifluoro-o-tolualdehyde, α,α,α-trifluoro-m-tolualdehyde, α,α,α-trifluoro-p-tolualdehyde, 3-fluorobenzaldehyde, 3-chlorobenzaldehyde, 4-fluorobenzaldehyde, 4-chlorobenzaldehyde, o-tolualdehyde, m-tolualdehyde, p-tolualdehyde, 3-fluoro-2-methylbenzaldehyde, 2-fluoro-3-(trifluoromethyl) benzaldehyde, 3,4-difluorobenzaldehyde, 2,3-difluorobenzaldehyde, 3-fluoro-p-anisaldehyde, 2,4-dimethoxybenzaldehyde, 2,5-dimethoxybenzaldehyde, 3,4-dimethoxybenzaldehyde, piperonal, 1,4-benzodioxane-6-carbaldehyde, 3,5-bis(trifluoromethyl)benzaldehyde, 3,5-dimethoxybenzaldehyde, 2,3-dimethyl-p-anisaldehyde, 2,3,4-trimethoxybenzaldehyde, 3,4,5-trimethoxybenzaldehyde, 2,4,5-trimethoxybenzaldehyde, 2,4,6-trimethoxybenzaldehyde, etc. may be used.

Step 10:

[0099] Using the similar method as in step 9, the compound (Io) of the general formulas (I), (I'), and (I") wherein A is a connecting bond, B is a methylene group, and Z is CH:

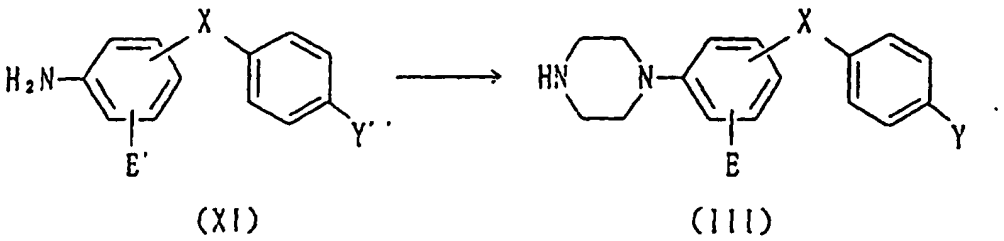


(Io)

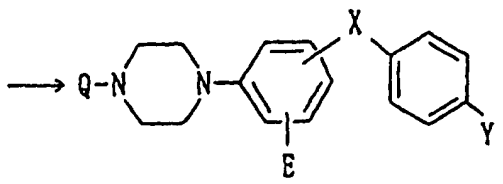
wherein, E, R", X, and Y are as defined above can be synthesized from the compound (IIi) obtained in step 2.

Step 11:

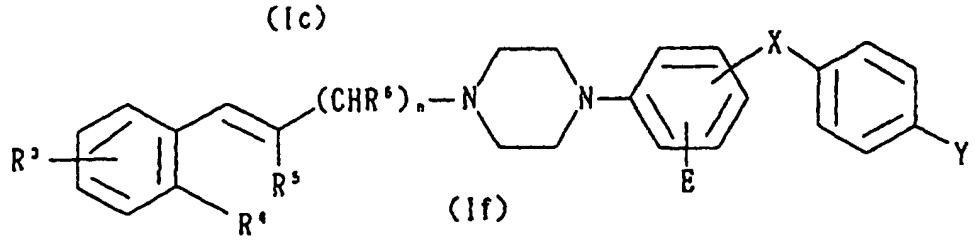
[0100] The compounds (Ic), (If), or (Ii) having the general formula (I) wherein Z is a nitrogen atom or the compound (I"') having the general formula (I') wherein Z is a nitrogen atom:



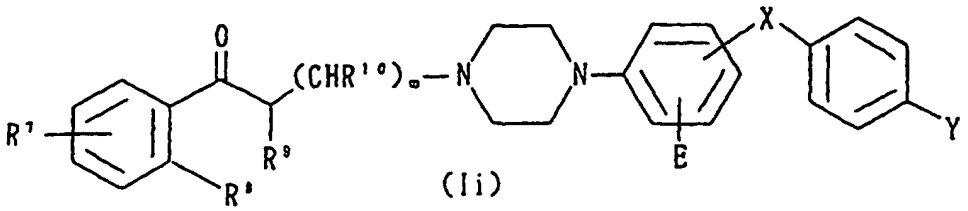
(XI) (III)



(Ic)

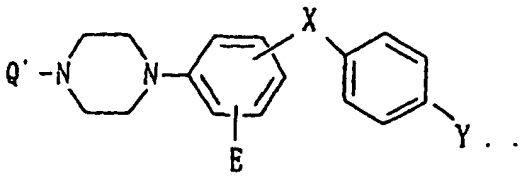


(If)



(Ii)

or



(I''')

(wherein, Q, Q', E, E', X, Y, Y'', R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, n, and m are as defined above) can be synthesized from the known starting material (X I).

[0101] That is, by causing the aniline derivative having the general formula (XI) to react under non-solvent conditions or in n-butanol, tert-butylalcohol or another solvent not participating in the reaction at 80°C to 300°C, preferably 150°C to 250°C, with 1 to 1.5 equivalents of a known bis-2-chloroethylamine hydrochloride for 1 to 12 hours, the compound of the general formula (III) can be obtained.

[0102] The starting material (XI) usable in the present reaction may be a compound which is commercially available or known through the literature [K. Suzuki et al.: J. Org. Chem., 26, 2239 (1961)] or may be synthesized by a known method as described for example in Japanese Examined Patent Publication (Kokoku) No. 6-25191. For example, 2-phenoxyaniline, 3-phenoxyaniline, 4-phenoxyaniline, 2-benzylaniline, 4-benzylaniline, 4-(4-fluorophenyl)methylaniline, 2-(4-fluorophenyl)-methylaniline, 4-(4-methoxyphenyl)methylaniline, 2-(4-methoxyphenyl)methylaniline, 4-(4-chlorophenyl)-methylaniline, 2-(4-chlorophenyl)methylaniline, 4-(4-trifluorophenyl)methylaniline, 2-(4-trifluorophenyl)-methylaniline, 2-benzyl-5-methoxyaniline, 4-benzyl-3-methoxyaniline, 2-(4-fluorophenyl) methyl-5-methoxyaniline, 4-(4-fluorophenyl) methyl-3-methoxyaniline, 5-fluoro-2-(4-fluorophenyl) methylaniline, 3-fluoro-4-(4-fluorophenyl) methylaniline, 5-fluoro-2-(4-methoxyphenyl) methylaniline, 3-fluoro-4-(4-methoxyphenyl) methylaniline, 5-methoxy-2-(4-methoxyphenyl)methylaniline, 3-methoxy-4-(4-methoxyphenyl)methylaniline, etc. may be used.

[0103] Further in the reaction according to the present invention, if necessary, sodium hydrogencarbonate, potassium hydrogencarbonate, sodium carbonate, potassium carbonate or other inorganic bases may be added.

[0104] Further, the compound having the general formula (III) wherein E or Y is a hydroxyl group may be obtained by removing the protective group from the compound having the general formula (III) where E or Y is an alkoxy group using the various methods described in "Protective Groups in Organic Synthesis" (T.W. Greene, John Wiley & Sons Ltd.) etc.

[0105] The compound (III) obtained in the aforementioned reaction can be used as it is for the next step, but can also be used after purification if necessary by a generally used purification method such as recrystallization or column chromatography etc.

[0106] The resultant compound (III) can be converted to the aryl piperadine derivatives having the general formulas (Ic), (If), (Ii), or (I''') by treating the said compound by the same methods as in, step 3, step 5, step 7, or step 9.

[0107] The isomers included in the compounds having the general formulas (I), (I'), (I''), and (I''') of the present invention may be separated by ordinary methods, for example, recrystallization, column chromatography, thin layer chromatography, high pressure liquid chromatography, or the similar methods using optically active reagents.

[0108] The compound having general formulas (I), (I'), (I"), and (I"') according to the present invention may be dissolved in a suitable organic solvent, for example, ether, tetrahydrofuran, methylene chloride, chloroform, benzene, toluene, etc. and treated by an inorganic or organic acid to obtain the corresponding salt. The inorganic acid used here include hydrochloric acid, sulfuric acid, nitric acid, phosphoric acid, periodic acid, and the like and the organic acid include formic acid, acetic acid, lactic acid, oxalic acid, malonic acid, propionic acid, valeric acid, succinic acid, fumaric acid, maleic acid, citric acid, malic acid, benzoic acid, p-toluenesulfonic acid, methanesulfonic acid, and the like.

[0109] The compounds having the general formula (I), (I'), (I") and (I"') of the present invention are low in toxicity and can be used alone by themselves or if desired can be prepared with other normal pharmaceutically allowable known and generally used carriers into preparations designed for the alleviation and treatment of symptoms based on ischemic diseases and symptoms derived from seizures, epilepsy, and migraine. For example, the effective ingredient can be administered orally or nonorally by itself or made into a capsule, tablet, injection, or other suitable preparation together with usually used excipients. For example, capsule preparations are prepared by mixing the powder with lactose, starch or its derivatives, cellulose derivatives or other excipients and packing the mixture into gelatin capsules. Further, tablets can be prepared by adding and kneading in, in addition to said excipient, sodium carboxycarboxymethylcellulose, alginic acid, arabia gum, and other binders and water, if necessary granulating the same, then further adding talc, stearic acid, and other lubricants and preparing the final form using a usual compression tablet-making machine. At the time of non-oral administration using injection, the effective ingredient is dissolved together with a solubilizer in sterilized distilled water or sterilized physiological saline and sealed in an ampule to make the injection preparation. If necessary, a stabilizing agent, buffer, etc. may also be included.

[0110] The dosage of the medicine for alleviation or treatment of symptoms based on ischemic diseases and symptoms derived from seizures, epilepsy and migraine of the present invention depends on various factors, for example, the symptoms and age of the patient to be treated, the route of administration, the form of the preparation, the frequency of administration, etc., but usually is 0.1 to 1000 mg/day/person, preferably 1 to 500 mg/day/person.

EXAMPLES

[0111] The present invention will now be explained in further detail with reference to Reference Examples and Examples, but the present invention is of course not limited in scope to these Examples.

Reference Example 1: Synthesis of N-tert-butoxycarbonyl-4-(4-phenoxyphenyl)-4-piperidinol (1) (Note: Table 1 Compound No. 1 (same below))

[0112] To a 100 ml tetrahydrofuran solution of 3.5 g of N-tert-butoxycarbonyl-4-piperidone was added dropwise, under ice cooling, 35 ml of 4-phenoxyphenyl magnesium bromide (0.6 mol/l tetrahydrofuran solution) prepared from 4-bromodiphenylether. This was stirred for 1 hour. To the reaction mixture was added 30 ml of a saturated aqueous solution of ammonium chloride. This was then extracted with ether. The extract was washed with saturated saline, dried, filtered, then concentrated under reduced pressure to obtain a residue which was then purified by silica gel column chromatography (hexane:ethyl acetate = 3:1) to obtain the above-referenced compound (1) in an amount of 2.92 g (yield 45%).

Reference Example 2: Synthesis of N-tert-butoxycarbonyl-4-[4-(4-fluorophenyl)methylphenyl]-4-piperidinol (2)

[0113] To a 25 ml ether solution of 2.5 g of 4-bromo-4'-fluorodiphenylmethane was gradually added dropwise at -78°C 6.5 ml of n-butyl lithium (1.6 mol/l hexane solution). This was warmed up to -20°C and stirred for 1 hour, then an 8 ml tetrahydrofuran solution of 1.8 g of N-tert-butoxycarbonyl-4-piperidone was added dropwise. This was stirred at 0°C for one hour, then 15 ml of a saturated aqueous solution of ammonium chloride was added and extraction was performed with ether. The extract was washed with saturated saline, dried, filtered, then concentrated under reduced pressure to obtain a residue, which was then purified by silica gel column chromatography (hexane:ethyl acetate = 4:1) to obtain the above-referenced compound (2) in an amount of 2.69 g (yield 77%).

Reference Example 3: Synthesis of N-tert-butoxycarbonyl-4-[3-(4-fluorophenyl)methylphenyl]-4-piperidinol (3)

[0114] The same procedure was followed as in Reference Example 2 using 3-bromo-4'-fluorodiphenylmethane to produce the above.

Reference Example 4: Synthesis of N-tert-butoxycarbonyl-4-[4-(4-methoxyphenyl)methylphenyl]-4-piperidinol (4)

[0115] The same procedure was followed as in Reference Example 2 using 4-bromo-4'-methoxydiphenylmethane

to produce the above.

Reference Example 5: Synthesis of (E)-1-[3-(4-hydroxy-3-methoxyphenyl)-1-oxo-2-propenyl]-4-(4-phenoxyphenyl) piperidine (5)

[0116] To a 25 ml methylene chloride solution of 0.95 g of 4-hydroxy-3-methoxycinnamic acid and 1.24 g of the compound (9) synthesized in Example 2 was added under ice cooling 1.41 g of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride, then the resulting mixture was stirred at room temperature for two hours. The reaction was washed with saturated saline, dried, filtered, then concentrated under reduced pressure to obtain a residue which was then purified by silica gel column chromatography (hexane:ethyl acetate = 3:1) to obtain the above-referenced compound (5) in an amount of 1.62 g (yield 91%).

Reference Example 6: Synthesis of (E)-1-[3-(4-hydroxy-3-methoxyphenyl)-1-oxo-2-propenyl]-4-4-phenoxyphenyl)-1,2,3,6-tetrahydropyridine (6)

[0117] The same procedure was followed as in Reference Example 5 using the compound (8) synthesized in Example 1 to produce the above.

Reference Example 7: Synthesis of (E)-4-[4-(4-fluorophenyl)methylphenyl]-1-[3-(4-hydroxy-3-methoxyphenyl)-1-oxo-2-propenyl]piperazine (7)

[0118] The same procedure was followed as in Reference Example 5 using the compound (10) synthesized in Example 3 to produce the above.

Example 1: Synthesis of 4-(4-phenoxyphenyl)-1,2,3,6-tetrahydropyridine (8)

[0119] To a 3 ml methylene chloride solution 772 mg of the compound (1) synthesized in Reference Example 1 was added dropwise under ice cooling 3 ml of trifluoroacetic acid. The resulting mixture was stirred at room temperature for two hours, then was adjusted by a 10% aqueous solution of sodium hydroxide to a pH = 9 to 10 and extracted with ether. The extract was dried, filtered, then concentrated under reduced pressure to obtain a crude crystal which was then recrystallized from ether/methylene chloride to obtain the above-referenced compound (8) in an amount of 250 mg (yield 47%).

Example 2: Synthesis of 4-(4-phenoxyphenyl)-piperidine (9)

[0120] To a 100 ml methanol solution of 3.51 g of the compound (8) synthesized in Example 1 were added 200 mg of palladium carbon and 1 ml of acetic acid for hydrogenation at atmospheric pressure and room temperature. After the completion of the reaction, the insolubles were filtered off, then the filtrate was concentrated under reduced pressure. The obtained residue was dissolved in methylene chloride and adjusted by a 10% aqueous solution of sodium hydroxide to a pH 9 to 10, then was shaken. The organic layer was dried, filtered, then condensed under reduced pressure to obtain a residue which was then purified by silica gel column chromatography (methylene chloride:methanol = 20:1) to obtain the above-referenced compound (9) in an amount of 2.32 g (yield 66%).

Example 3: Synthesis of 1-[4-(4-fluorophenyl) methylphenyl]piperazine (10)

[0121] A mixture of 500 mg of 4-(4-fluorophenyl)-methylaniline and 445 mg of bis(2-chloroethyl)amine hydrochloride was stirred at 100°C for two hours, then gradually raised in temperature and stirred at 200°C for a further two hours. This was cooled to room temperature, then the product was purified by silica gel column chromatography (chloroform: methanol:water (2% acetic acid) = 65:35:5) to obtain the above-referenced compound (10) in an amount of 503 mg (yield 75%).

Example 4: Synthesis of 4-[4-(4-fluorophenyl)-methylphenyl]-1,2,3,6-tetrahydropyridine (11)

[0122] The same procedure was followed as in Example 1 using the compound (2) synthesized in Reference Example 2 to produce the above.

Example 5: Synthesis of 4-[4-(4-fluorophenyl)-methylphenyl]piperidine (12)

[0123] The same procedure was followed as in Example 2 using the compound (11) synthesized in Example 4 to produce the above.

Example 6 : Synthesis of 4-[3-(4-fluorophenyl)-methylphenyl]-1,2,3,6-tetrahydropyridine (13) (Reference)

[0124] The same procedure was followed as in Example 1 using the compound (3) synthesized in Reference Example 3 to produce the above.

Example 7: Synthesis of 4-[3-(4-fluorophenyl)-methylphenyl]piperidine (14) (Reference)

[0125] The same procedure was followed as in Example 2 using the compound (13) synthesized in Example 6 to produce the above.

Example 8: Synthesis of 1-[2-(4-fluorophenyl)-methylphenyl]piperazine (15) (Reference)

[0126] The same procedure was followed as in Example 3 using 2-(4-fluorophenyl)methylaniline to produce the above.

Example 9: Synthesis of 4-[4-(4-methoxyphenyl) methylphenyl]-1,2,3,6-tetrahydropyridine (16)

[0127] The same procedure was followed as in Example 1 using the compound (4) synthesized in Reference Example 4 to produce the above.

Example 10: Synthesis of 4-[4-(4-methoxyphenyl) methylphenyl]piperidine (17)

[0128] The same procedure was followed as in Example 2 using the compound (16) synthesized in Example 9 to produce the above.

Example 11: Synthesis of (E)-4-(4-phenoxyphenyl)-1-(3-phenyl-2-propenyl)-1,2,3,6-tetrahydropyridine (18)

[0129] To an 8 ml acetonitrile solution of 300 mg of the compound (8) synthesized in Example 1 were added 234 mg cinnamyl bromide and 0.5 ml of triethylamine. This was then heated and refluxed for 3 hours. To the reaction mixture was added 10 ml of ice water. This was then extracted with ethyl acetate. The extract was dried, filtered, then concentrated under reduced pressure to obtain a residue which was then purified by silica gel column chromatography (methylene chloride:methanol = 25:1) to obtain the above-referenced compound (18) in an amount of 320 mg (yield 73%).

Example 12: Synthesis of (E)-1-[3-(4-hydroxy-3-methoxyphenyl)-2-propenyl]-4-(4-phenoxyphenyl)piperidine (19)

[0130] To an 8 ml tetrahydrofuran solution of 400 mg of the compound (5) synthesized in Reference Example 5 was added under ice cooling 60 mg of lithium aluminum hydride, then the resulting mixture was stirred at room temperature for two hours. A 10% aqueous solution of sodium hydroxide solution was added, then the product was extracted with methylene chloride. The extract was dried, filtered, then concentrated under reduced pressure to obtain a residue which was then purified by silica gel column chromatography (methylene chloride:methanol = 20:1) to obtain the above-referenced compound (19) in an amount of 273 mg (yield 72%).

Example 13: Synthesis of 1-[2-(4-fluorophenyl) oxyethyl]-4-(4-phenoxyphenyl]-1,2,3,6-tetrahydropyridine (20)

[0131] The same procedure was followed as in Example 11 using the compound (8) synthesized in Example 1 and 2-(4-fluorophenyl)oxyethyl bromide to produce the above.

Example 14: Synthesis of (E)-4-(4-phenoxyphenyl)-1-(3-phenyl-2-propenyl)piperidine (21)

[0132] The same procedure was followed as in Example 11 using the compound (9) synthesized in Example 2 and cinnamyl bromide to produce the above.

Example 15: Synthesis of 4-(4-phenoxyphenyl)-1-(3-phenylpropyl)piperidine (22)

[0133] The same procedure was followed as in Example 11 using the compound (9) synthesized in Example 2 and 1-bromo-3-phenylpropane to produce the above.

Example 16: Synthesis of 4-(4-phenoxyphenyl)-1-[3-(2,3,4-trimethoxyphenyl)-2-propenyl]piperidine (23)

[0134] The same procedure was followed as in Example 11 using the compound (9) synthesized in Example 2 and (2,3,4-trimethoxy)cinnamyl bromide to produce the above.

Example 17: Synthesis of (E)-1-[3-(4-hydroxy-3-methoxyphenyl)-2-propenyl]-4-(4-phenoxyphenyl)-1,2,3,6-tetrahydropyridine (24)

[0135] The same procedure was followed as in Example 12 using the compound (6) synthesized in Reference Example 6 to produce the above.

Example 18: Synthesis of (E)-1-[3-(4-fluorophenyl)-2-propenyl]-4-(4-phenoxyphenyl)piperidine (25).

[0136] The same procedure was followed as in Example 11 using the compound (9) synthesized in Example 2 and 4-fluorocinnamyl bromide to produce the above.

Example 19: Synthesis of 4-(phenoxyphenyl)-1-[trans- (2-phenyl)cyclopropylmethyl]piperidine (26)

[0137] The same procedure was followed as in Example 11 using the compound (9) synthesized in Example 2 and trans-(2-phenyl)cyclopropylmethyl bromide to produce the above.

Example 20: Synthesis of 1-[2-(4-fluorophenyl) oxyethyl]-4-(4-phenoxyphenyl)piperidine (27)

[0138] The same procedure was followed as in Example 11 using the compound (9) synthesized in Example 2 and 2-(4-fluorophenyl)oxyethyl bromide to produce the above.

Example 21: Synthesis of 1-[4-(4-fluorophenyl)-oxybutyl]-4-(4-phenoxyphenyl)piperidine (28)

[0139] The same procedure was followed as in Example 11 using the compound (9) synthesized in Example 2 and 2-(4-fluorophenyl)oxybutyl bromide to produce the above.

Example 22: Synthesis of 4-(4-phenoxyphenyl)-1-[(2,3,4-trimethoxyphenyl]methyl]piperidine (29)

[0140] A mixture of 1.27 g of the compound (9) synthesized in Example 2 and 0.8 g of 2,3,4-trimethoxybenzaldehyde was stirred at 120°C, then, 0.18 ml of formic acid was added dropwise. This was stirred for one hour at the same temperature, then ethyl acetate and a saturated aqueous solution of sodium hydrogencarbonate were added and the results were shaken. The organic layer was dried, filtered, then concentrated under reduced pressure to obtain a residue which was then purified by silica gel column chromatography (hexane:ethyl acetate = 3:2) to obtain the above-referenced compound (29) in an amount of 1.46 g (yield 73%).

Example 23: Synthesis of 1-[4-((4-fluorophenyl)-4-oxo)butyl]-4-(4-phenoxyphenyl)piperidine (30)

[0141] To a 6 ml dimethylformamide solution of 350 mg of the compound (9) synthesized in Example 2 were added 278 mg of 4-chloro-4'-fluorobutylophenone, 230 mg of potassium carbonate, and 415 mg of sodium iodide, then the mixture was stirred at 80°C for 2 hours. 15 ml of ice water was added, then the product was extracted with ethyl acetate. The extract was washed with saturated saline, dried, filtered, then concentrated under reduced pressure to obtain a residue, which was then purified by silica gel column chromatography (methylene chloride:methanol = 20:1) to obtain the above-referenced compound (30) in an amount of 392 mg (yield 68%).

Example 24: Synthesis of (E)-4-[4-(4-fluorophenyl)-methylphenyl]-1-(3-phenyl-2-propenyl)-1,2,3,6-tetrahydropyridine (31)

[0142] The same procedure was followed as in Example 11 using the compound (11) synthesized in Example 4 to

produce the above.

Example 25: Synthesis of (E)-4-[4-(4-fluorophenyl) methylphenyl]-1-(3-phenyl-2-propenyl)piperidine (32)

[0143] The same procedure was followed as in Example 11 using the compound (12) synthesized in Example 5 to produce the above.

Example 26: Synthesis of 4-[4-(4-fluorophenyl) methylphenyl]-1-[trans-(2-phenyl)cyclopropylmethyl]-piperidine (33)

[0144] The same procedure was followed as in Example 11 using the compound (12) synthesized in Example 5 and trans-(2-phenyl)cyclopropylmethyl bromide to produce the above.

Example 27: Synthesis of (E)-4-[2-(4-fluorophenyl) methylphenyl]-1-(3-phenyl-2-propenyl)-1,2,3,6-tetrahydropyridine (34) (Reference)

[0145] The same procedure was followed as in Example 11 using 4-[2-(4-fluorophenyl)methylphenyl]-1,2,3,6-tetrahydropyridine and cinnamyl bromide to produce the above.

Example 28: Synthesis of (E)-4-[2-(4-fluorophenyl) methylphenyl]-1-(3-phenyl-2-propenyl)piperidine (35) (Reference)

[0146] The same procedure was followed as in Example 11 using 4-[2-(4-fluorophenyl)methylphenyl]piperidine to produce the above.

Example 29: Synthesis of 4-[2-(4-fluorophenyl)-methylphenyl]-1-[trans-(2-phenyl)cyclopropylmethyl]-piperidine (36) (Reference)

[0147] The same procedure was followed as in Example 11 using 4-[2-(4-fluorophenyl)methylphenyl]piperidine and trans-(2-phenyl)cyclopropylmethyl bromide to produce the above.

Example 30: Synthesis of (E)-4-[3-(4-fluorophenyl)-methylphenyl]-1-(3-phenyl-2-propenyl)-1,2,3,6-tetrahydropyridine (37) (Reference)

[0148] The same procedure was followed as in Example 11 using the compound (13) synthesized in Example 6 to produce the above.

Example 31: Synthesis of (E)-4-[3-(4-fluorophenyl)-methylphenyl]-1-(3-phenyl-2-propenyl)piperidine (38) (Reference)

[0149] The same procedure was followed as in Example 11 using the compound (14) synthesized in Example 7 to produce the above.

Example 32: Synthesis of 4-[3-(4-fluorophenyl)-methylphenyl]-1-[trans-(2-phenyl)cyclopropylmethyl]-piperidine (39) (Reference)

[0150] The same procedure was followed as in Example 11 using the compound (14) synthesized in Example 7 and trans-(2-phenyl) cyclopropylmethyl bromide to produce the above.

Example 33: Synthesis of (E)-1-(4-phenoxyphenyl)-4-(3-phenyl-2-propenyl)piperazine (40)

[0151] The same procedure was followed as in Example 11 using the 1-(4-phenoxyphenyl)piperazine [US4210646; DT2631885] to produce the above.

Example 34: Synthesis of 4-[4-(4-fluorophenyl)-oxybutyl]-1-(4-phenoxyphenyl)piperazine (41)

[0152] The same procedure was followed as in Example 11 using the 1-(4-phenoxyphenyl)piperazine and 2-(4-fluorophenyl)oxybutyl bromide to produce the above.

Example 35: Synthesis of (E)-1-(2-phenoxyphenyl)-4-(3-phenyl-2-propenyl)piperazine (42) (Reference)

[0153] The same procedure was followed as in Example 11 using 1-(2-phenoxyphenyl)piperazine [DT2631885] to produce the above.

Example 36: Synthesis of 1-(2-phenoxyphenyl)-4-[trans-(2-phenyl)cyclopropylmethyl]piperazine (43) (Reference)

[0154] The same procedure was followed as in Example 11 using the 1-(2-phenoxyphenyl)piperazine and trans-(2-phenyl)cyclopropylmethyl bromide to produce the above.

Example 37: Synthesis of (E)-1-[3-phenoxyphenyl)-4-(3-phenyl-2-propenyl)piperazine (44) (Reference)

[0155] The same procedure was followed as in Example 11 using 1-(3-phenoxyphenyl)piperazine [DT2631885] to produce the above.

Example 38: Synthesis of 1-(3-phenoxyphenyl)-4-[trans-(2-phenyl)cyclopropylmethyl]piperazine (45) (Reference)

[0156] The same procedure was followed as in Example 11 using 1-(3-phenoxyphenyl)piperazine and trans-(2-phenyl)-cyclopropylmethyl bromide to produce the above.

Example 39: Synthesis of 1-(4-phenoxyphenyl)-4-[(2,3,4-trimethoxyphenyl)methyl]piperazine (46)

[0157] The same procedure was followed as in Example 22 using 1-(4-phenoxyphenyl) piperazine to produce the above.

Example 40: Synthesis of (E)-1-[4-(4-fluorophenyl) methylphenyl]-1-(3-phenyl-2-propenyl)piperazine (47)

[0158] The same procedure was followed as in Example 11 using the compound (10) synthesized in Example 3 to produce the above.

Example 41: Synthesis of (E)-1-[4-(4-fluorophenyl)-methylphenyl]-1-[3-(2,3,4-trimethoxyphenyl)-2-propenyl]-pioerazine (48)

[0159] The same procedure was followed as in Example 11 using the compound (10) synthesized in Example 3 and (2,3,4-trimethoxy) cinnamyl bromide to produce the above.

Example 42: Synthesis of (E)-1-[4-(4-fluorophenyl)-methylphenyl]-4-4-[3-(4-hydroxy-3-methoxyphenyl)-2-propenyl] piperazine (49)

[0160] The same procedure was followed as in Example 12 using the compound (7) synthesized in Reference Example 7 to produce the above.

Example 43: Synthesis of (E)-1-[4-(4-fluorophenyl) methylphenyl]-4-[3-(4-fluorophenyl)-2-propenyl]-piperazine (50)

[0161] The same procedure was followed as in Example 11 using the compound (10) synthesized in Example 3 and 4-fluorocinnamyl bromide to produce the above.

Example 44: Synthesis of (E)-1-(2-benzylphenyl)-4-(3-phenyl-2-propenyl)piperazine (51) (Reference)

[0162] The same procedure was followed as in Example 11 using the 1-(2-benzylphenyl)piperazine [Japanese Examined Patent Publication (Kokoku) No. 6-25191] to produce the above.

Example 45: Synthesis of (E)-1-(2-benzylphenyl)-4-[trans-(2-phenyl)cyclopropylmethyl]piperazine (52) (Reference)

[0163] The same procedure was followed as in Example 11 using 1-(2-benzylphenyl)piperazine and trans-(2-phenyl)-cyclopropylmethyl bromide to produce the above.

Example 46 : Synthesis of (E)-1-[2-(4-fluorophenyl) methylphenyl]-4-(3-phenyl-2-propenyl)piperazine (53) (Reference)

[0164] The same procedure was followed as in Example 11 using the compound (15) synthesized in Example 8 to produce the above.

Example 47: Synthesis of (E)-1-[2-(4-fluorophenyl) methylphenyl]-4-[trans-(2-phenyl)cyclopropylmethyl]-piperazine (54) (Reference)

[0165] The same procedure was followed as in Example 11 using the compound (15) synthesized in Example 8 and trans-(2-phenyl)cyclopropylmethyl bromide to produce the above.

Example 48: Synthesis of (E)-1-[4-(4-fluorophenyl)-methylphenyl]-4-[trans-(2-phenyl)cyclopropylmethyl]-piperazine (55)

[0166] The same procedure was followed as in Example 11 using the compound (10) synthesized in Example 3 and trans-(2-phenyl) cyclopropylmethyl bromide to produce the above.

Example 49: Synthesis of 1-[4-(4-fluorophenyl)-methylphenyl]-4-[(2,3,4-trimethoxyphenyl)methyl] piperazine (56)

[0167] The same procedure was followed as in Example 22 using the compound (10) synthesized in Example 3 to produce the above.

Example 50: Synthesis of 4-[4-(4-fluorophenyl)-oxvbutyl]-1-[4-(4-fluorophenyl)methylphenyl]piperazine (57)

[0168] The same procedure was followed as in Example 11 using the compound (10) synthesized in Example 3 and 4-(4-fluorophenyl)oxybutyl bromide to produce the above.

Example 51: Synthesis of 1-[4-(4-fluolophenyl) methylphenyl]-4-[4-((4-fluorophenyl)-4-oxo)butyl]-piperazine (58)

[0169] The same procedure was followed as in Example 23 using the compound (10) synthesized in Example 3 to produce the above.

Example 52: Synthesis of 4-(4-phenoxyphenyl)-1-(1-phenyl-1-cyclopropane)methylpiperidine (59)

[0170] The same procedure was followed as in Example 11 using the compound (9) synthesized in Example 2 and 1-phenyl-1-cyclopropanemethyl bromide to produce the above.

Example 53: Synthesis of 1-ethyl-4-(4-phenoxyphenyl) piperidine (60)

[0171] The same procedure was followed as in Example 11 using the compound (9) synthesized in Example 2 and ethyl iodide to produce the above.

Example 54: Synthesis of 1-[4-(4-fluorophenyl) methylphenyl]-4-methylpiperazine (61)

[0172] The same procedure was followed as in Example 11 using the compound (10) synthesized in Example 3 and methyl iodide to produce the above.

Example 55: Synthesis of 4-[4-(4-fluorophenyl)-methylphenyl]-1-(1-phenyl-1-cyclopropane)methyl piperidine (62)

[0173] The same procedure was followed as in Example 11 using the compound (12) synthesized in Example 5 and 1-phenyl-1-cyclopropanemethyl bromide to produce the above.

Example 56: Synthesis of 4-[4-(4-fluorophenyl) methylphenyl]-1-(2-phenyl-2-oxo)ethylpiperidine (63)

[0174] The same procedure was followed as in Example 11 using the compound (12) synthesized in Example 5 and phenacyl bromide to produce the above.

Example 57: Synthesis of 4-(4-phenoxyphenyl)-1-(2-phenyl-2-oxo)ethylpiperidine (64)

[0175] The same procedure was followed as in Example 11 using the compound (9) synthesized in Example 2 and phenacyl bromide to produce the above.

Example 58: Synthesis of 4-[4-(4-fluorophenyl) methylphenyl]-1-(1-phenyl-1-cyclopropyl)methylpiperidine (65)

[0176] The same procedure was followed as in Example 11 using the compound (12) synthesized in Example 5 and 1-phenyl-1-cyclopropylmethyl bromide to produce the above.

Example 59: Synthesis of 1-[2-(4-methoxyphenyl)-2-oxo]ethyl-4-(4-phenoxyphenyl)piperidine (66)

[0177] The same procedure was followed as in Example 11 using the compound (9) synthesized in Example 2 and 2-bromo-4'-methoxyacetophenone to produce the above.

Example 60: Synthesis of 1-[2-(4-fluorophenyl)-2-oxo]ethyl-4-(4-phenoxyphenyl)piperidine (67)

[0178] The same procedure was followed as in Example 11 using the compound (9) synthesized in Example 2 and 2-bromo-4'-fluoroacetophenone to produce the above.

Example 61: Synthesis of 1-[2-(4-chlorophenyl)-2-oxo]ethyl-4-(4-phenoxyphenyl)piperidine (68)

[0179] The same procedure was followed as in Example 11 using the compound (9) synthesized in Example 2 and 2-bromo-4'-chloroacetophenone to produce the above.

Example 62: Synthesis of 1-(1-benzoylethyl)-4-(4-phenoxyphenyl)piperidine (69)

[0180] The same procedure was followed as in Example 11 using the compound (9) synthesized in Example 2 and 2-bromopropiophenone to produce the above.

Example 63 : Synthesis of 4-[4-(4-methoxyphenyl) methylphenyl]-1-(2-phenyl-2-oxo)ethylpiperidine (70)

[0181] The same procedure was followed as in Example 11 using the compound (17) synthesized in Example 10 and phenacyl bromide to produce the above.

Example 64: Synthesis of 1-(1-oxoindan-2-yl)-4-(4-phenoxy)phenylpiperidine (71)

[0182] The same procedure was followed as in Example 11 using the compound (9) synthesized in Example 2 and 2-bromo-1-indanone to produce the above.

Example 65: Synthesis of 4-[4-(4-fluorophenyl) methylphenyl]-1-(1-oxoindan-2-yl)piperidine (72)

[0183] The same procedure was followed as in Example 11 using the compound (12) synthesized in Example 5 and 2-bromo-1-indanone to produce the above.

Example 66: Synthesis of 2-[4-(4-phenoxyphenyl) piperidin-1-yl]methyl-2-phenyl-1,3-dioxolane (73)

[0184] The same procedure was followed as in Example 11 using the compound (9) synthesized in Example 2 and 2-bromomethyl-2-phenyl-1,3-dioxolane to produce the above.

Example 67: Synthesis of 4-(4-phenoxyphenyl)-1-(2-phenyl-2-hydroxyimino)ethylpiperidine (74)

[0185] An 8 ml pyridine solution of 500 mg of the compound (64) synthesized in Example 57 and 96 mg of hydroxyamine hydrochloride was stirred for one hour at 100°C. To the reaction mixture was added 10 ml of ice water, then the product was extracted with ethyl acetate. The extract was washed with saturated saline, dried, filtered, then concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (methylene chloride:methanol = 20:1) to obtain the above-referenced compound (74) in an amount of 437 mg (yield 84%).

Example 68: Synthesis of 4-[4-(4-methoxyphenyl] methylphenyl]-(E)-1-(3-phenyl-2-propenyl)piperidine (75)

[0186] The same procedure was followed as in Example 11 using the compound (17) synthesized in Example 10 to produce the above.

Example 69: Synthesis of 1-(benzofuran-2-yl)methyl-4-(4-phenoxyphenyl)piperidine (76)

[0187] The same procedure was followed as in Example 11 using the compound (9) synthesized in Example 2 and 2-bromomethylbenzofuran to produce the above.

Example 70: Synthesis of 1-(2-hydroxy-2-phenyl) ethyl-4-(4-phenoxyphenyl)piperidine (77)

[0188] To 8 ml of a methanol solution of 450 mg of the compound (64) synthesized in Example 57 was gradually added 46 mg of sodium borohydride under ice cooling. The resulting mixture was stirred at room temperature for one hour. To the reaction was added 12 ml of ice water, then the product was extracted with ethyl acetate. The extract was washed with saturated saline, dried, filtered, then concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (methylene chloride:methanol = 20:1) so as to obtain the above-referenced compound (77) in an amount of 403 mg (yield 89%).

Example 71: Synthesis of 1-[2-(4-chlorophenyl)-2-hydroxy]ethyl-4-(4-phenoxyphenyl)piperidine (78)

[0189] The same procedure was followed as in Example 70 using the compound (68) synthesized in Example 61 to produce the above.

Example 72: Synthesis of 4-[4-(4-fluorophenyl) methylphenyl]-1-(2-hydroxy-2-phenyl)ethylpiperidine (79)

[0190] The same procedure was followed as in Example 70 using the compound (63) synthesized in Example 56 to produce the above.

Example 73: Synthesis of 1-(2-hydroxy-3-phenoxy)propyl-4-(4-phenoxyphenyl)piperidine (80)

[0191] A 10 ml isopropyl alcohol solution of 300 mg of the compound (9) synthesized in Example 2 and 165 mg of phenyl glycidyl ether was stirred at 100°C for two hours. The reaction was concentrated under reduced pressure to obtain a residue which was then purified by silica gel column chromatography (chloroform:methanol = 20:1) to obtain the above-referenced compound (80) in an amount of 399 mg (yield 90%).

Example 74: Synthesis of 4-[4-(4-fluorophenyl) methylphenyl]-1-(2-hydroxy-3-phenoxy)propylpiperidine (81)

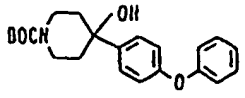
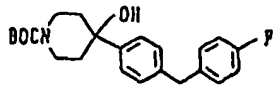
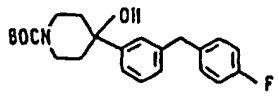
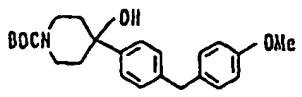
[0192] The same procedure was followed as in Example 73 using the compound (12) synthesized in Example 5 to produce the above.

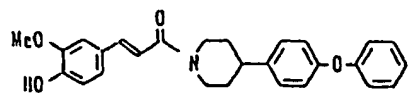
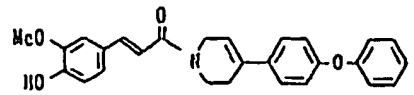
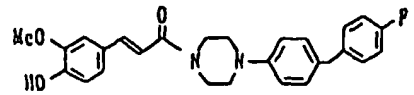
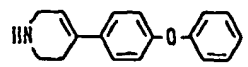
Example 75: Synthesis of 1-[4-(4-fluorophenyl) methylphenyl]-4-(2-phenyl-2-oxo)ethylpiperazine (82)

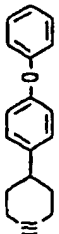
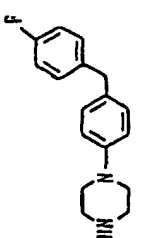
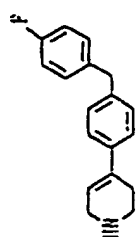
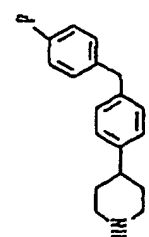
[0193] The same procedure was followed as in Example 11 using the compound (10) synthesized in Example 3 and phenacyl bromide to produce the above.

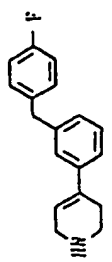
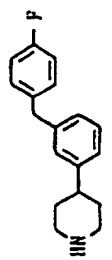
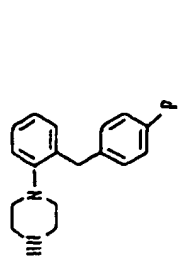
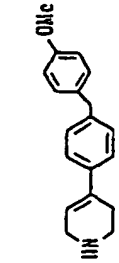
[0194] The physical properties of the compounds obtained in the above Reference Examples and Examples are shown in Table 1.

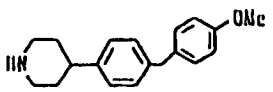
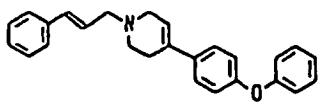
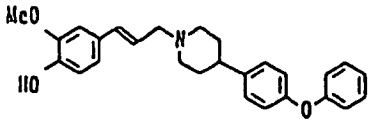
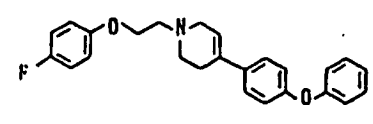
Table 1

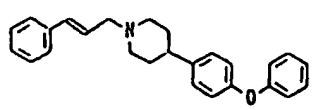
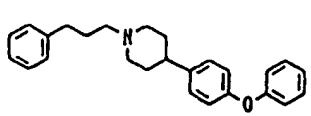
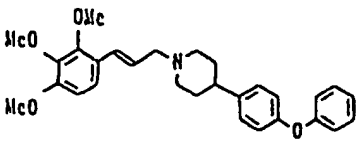
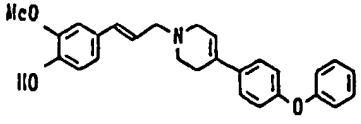
Compound no.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR (CDCl$_3$)	Elemental analysis
1		An oily substance	(CHCl$_3$) 3094. 3436. 3010. 2980. 2875. 1682. 1589. 1507. 1489. 1430. 1367. 1242. 1168	1.46(9H. s). 1.77-1.78(2H. m). 1.98(2H. t). 3.25(2H. t). 4.24(2H. m). 6.99(4H. m). 7.08-7.14(1H. m). 7.34(2H. m). 7.40-7.46(2H. m)	———
2		An oily substance	(CHCl$_3$) 3018. 1682. 1508. 1431. 1367. 1168	1.48(9H. s). 1.70-1.74(2H. m). 1.97(2H. t). 3.24(2H. t). 3.94(2H. s). 4.00(2H. m). 6.94-6.99(2H. m). 7.11-7.17 (4H. m). 7.38(2H. d)	———
3		An oily substance	(CHCl$_3$) 3468. 2979. 1684. 1508. 1426. 1162. 1032	1.47(9H. s). 1.6-1.7(2H. m). 1.96(2H. t). 3.25(2H. t). 3.95(2H. s). 6.9-7.45(8H. m)	———
4		An oily substance	(CHCl$_3$) 3019. 1676. 1509. 1225. 1206. 785. 772. 761. 750. 736. 672	1.42-1.49(9H. m). 1.72(2H. m). 1.98(2H. dt). 3.24(2H. dt). 3.78(3H. s). 3.91(2H. s). 3.98(2H. m). 6.83(2H. dd). 7.10(2H. d). 7.17(2H. d). 7.37(2H. dd)	———

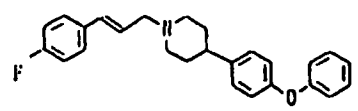
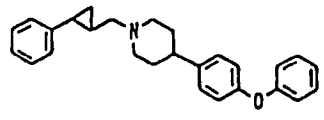
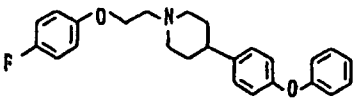
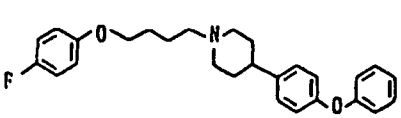
Compound no.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR ($CDCl_3$)	Elemental analysis
5		Colorless crystals 88-90°C (ethyl acetate/ hexane)	($CHCl_3$) 3020. 2400. 1644. 1594. 1509. 1489. 930	1.68(2H. ddd). 1.95(2H. d). 2.78(1H. t). 2.79(1H. brs). 3.22(1H. brs). 3.93(3H. s). 4.26(1H. brs). 4.89(1H. brs). 5.81(1H. s). 6.78(1H. d). 6.90-7.01(5H. m). 7.09-7.17(5H. m). 7.30-7.34 (2H. m). 7.62(1H. d)	$C_{21}H_{21}NO_4 \cdot 1/4H_2O$ C H N Calcd: 74.72 6.39 3.23 Found: 74.69 6.28 2.94
6		Colorless crystals 87-88°C (ethyl acetate/ hexane)	($CHCl_3$) 3020. 2402. 1641. 1590. 1508. 1490. 1438. 1376. 1034. 931	2.62(2H. m). 3.89(2H. m) 3.94(3H. s). 4.35(2H. m) 5.77(1H. s). 6.04(1H. m) 6.70-7.45(13H. m). 7.64(1H. d)	———
7		Colorless crystals 137-138°C (ethyl acetate/ hexane)	($CHCl_3$) 2364. 1644. 1609. 1513. 1456	3.19(4H. t). 3.84(4H. m). 3.88(2H. s). 3.94(3H. s). 5.77(1H. s). 6.74(1H. d). 6.86-7.00(6H. m). 7.07-7.14 (5H. m). 7.63(1H. d)	$C_{21}H_{21}FN_2O_3 \cdot 1/2H_2O$ C H N Calcd: 71.19 6.39 6.15 Found: 70.92 6.11 6.16
8		Colorless crystals 186-189°C (methylene chloride/ ether)	($CHCl_3$) 3024. 3018. 1674. 1606. 1508. 1489. 1243	2.45(2H. td). 3.11(2H. t). 3.53(2H. dd). 6.09(1H. m). 6.94-7.13(5H. m). 7.29-7.39 (4H. m)	———

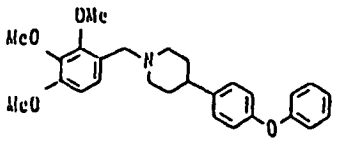
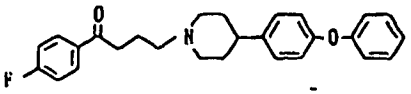
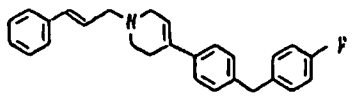
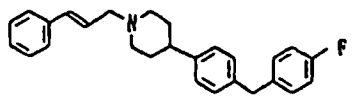
Compound No.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR ($CDCl_3$)	Elemental analysis
9		Colorless crystals (hydrochloride) 86-87°C (methylene chloride/ ether)	(KBr) (hydrochloride) 3024. 2960. 2712. 1590. 1508. 1489. 1241. 1208	1.61(2H, ddd). 1.83(2H, d). 2.60(1H, t). 2.74(2H, td). 3.18(2H, d). 6.94(2H, d). 7.00(2H, d). 7.07(1H, t). 7.17(2H, d). 7.31(2H, t)	———
10		Colorless crystals (dihydrochloride) 139-141°C (methanol/ ether)	(KBr) (dihydrochloride) 3426. 3410. 3000. 2636. 2480. 1602. 1508. 1221. 1158	3.03(4H, dd). 3.11(4H, dd). 3.87(2H, s). 6.83-7.14(8H, m)	———
11		Pale yellow crystals	($CHCl_3$) 3020. 2926. 2993. 1604. 1508. 1434. 1157. 1016. 930	2.43(2H, td). 3.09(2H, t). 3.51(2H, dd). 3.92(2H, s). 6.10(1H, m). 6.94-6.98(2H, m). 7.10-7.15(4H, m). 7.31(2H, d)	———
12		An oily substance	($CHCl_3$) 2930. 2337. 1603. 1508. 1446. 1318. 1016. 862. 820	1.57-1.66(2H, m). 1.83(2H, d). 2.58(1H, t). 2.73(2H, td). 3.17(2H, d). 3.91(2H, s). 6.94-6.97(2H, m). 7.08-7.18 (6H, m)	———

Compound no.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR (CDCl$_3$)	Elemental analysis
13		An oily substance	(CHCl$_3$) 2924. 1604. 1508. 1436. 1157. 1093	2.45(2H, m). 3.1(2H, t). 3.52(2H, m). 3.94(2H, s). 6.09(1H, t). 6.9-7.35(8H, m)	———
14		An oily substance	(CHCl$_3$) 2938. 1606. 1508. 1446. 1318. 1157. 1094. 928	1.66(2H, m). 1.83(2H, m). 2.6(1H, t). 2.75(2H, td). 3.2(2H, m). 3.96(2H, s). 6.9-7.4(8H, m)	———
15		An oily substance	(CHCl$_3$) 3020. 2400. 1508. 1489. 1156. 1135. 932. 848	2.80(4H, dd). 2.96(4H, dd). 4.04(2H, s). 6.91-7.23(8H, m)	———
16		Colorless crystals	(CHCl$_3$) 3020. 1508. 1226. 1212. 1208. 775. 708. 758. 752. 732	2.43(2H, m). 3.09(2H, t). 3.51(2H, dd). 3.78(3H, s). 3.90(2H, s). 6.09(1H, bs). 6.82(2H, d). 7.12(4H, dd). 7.29(2H, d)	———

Compound no.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR (CDCl$_3$)	Elemental analysis
17		An oily substance	(CHCl$_3$) 3023. 1654. 1560. 1508. 1227. 1203. 799. 722	1.62(2H. dt). 1.81(2H. d). 2.57(1H. tt). 2.72(2H. dt). 3.17(2H. m). 3.77(3H. s). 3.89(2H. s). 6.82(2H. d). 7.09-7.14(6H. m)	———
18		Colorless crystals (hydrochloride) 202-205°C (methanol/ ether)	(KBr) (hydrochloride) 2482. 1588. 1508. 1486. 1236. 1173. 980. 867. 821. 750. 692	2.59(2H. d). 2.78(2H. t). 3.22(2H. dd). 3.30(2H. dd). 6.03(1H. m). 6.36(1H. dt). 6.58(1H. d). 6.96(2H. dd). 7.01(2H. d). 7.10(1H. t). 7.24-7.41(9H. m)	$C_{21}H_{23}ClNO$ (hydrochloride)·1/4H_2O C H N Calcd: 76.46 6.54 3.43 Found: 76.19 6.41 3.48
19		Yellow crystals (hydrochloride) 103-106°C (methanol/ ether)	(KBr) (hydrochloride) 2934. 1653. 1594. 1508. 1490. 1281. 1234. 1170. 1124. 1032. 871. 749. 692	1.77-1.85(4H. m). 2.10(2H. dt). 2.53(1H. tt). 3.13-3.19(4H. m). 3.90(3H. s). 5.66(1H. brs). 6.17(1H. dt). 6.46(1H. d). 6.86-7.00(6H. m). 7.07(1H. t). 7.18(2H. d). 7.29-7.33(2H. m)	$C_{21}H_{23}ClNO_2$(hydrochloride)·7/5H_2O C H N Calcd: 67.96 6.93 2.94 Found: 67.88 6.66 2.95
20		Colorless crystals (hydrochloride) 163-165°C (methanol/ ether)	(KBr) (hydrochloride) 2936. 2700. 2594. 1589. 1509. 1492. 1243. 1053. 827	2.59(2H. m). 2.85(2H. t). 2.93(2H. t). 3.3(2H. dd). 4.14(2H. t). 6.02(1H. t). 6.8-7.15(9H. m). 7.32(2H. d). 7.36(2H. d)	$C_{21}H_{23}ClFNO_2$(hydrochloride) C H N Calcd: 70.50 5.92 3.29 Found: 70.01 5.78 3.30

Compound no.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR ($CDCl_3$)	Elemental analysis
21		Colorless crystals (hydrochloride) 200-204°C (methanol/ ether)	(KBr) (hydrochloride) 2930. 2520. 1654. 1589. 1504. 1490. 1239. 1170. 978. 869. 749. 693	1.75-1.87(4H, m), 2.10(2H, dt). 2.50(1H, tt). 3.12(2H, d). 3.20(2H, d). 6.34(1H, dt). 6.55(1H, d). 6.94(2H, d). 6.99(2H, d). 7.07(1H, t). 7.19(2H, d). 7.22-7.33(5H, m). 7.39(2H, d)	$C_{21}H_{24}ClNO$ (hydrochloride) C 76.92 H 6.95 N 3.45 Calcd; 76.77 6.95 3.45 Found;
22		Colorless crystals (hydrochloride) 199-201°C (methanol/ ether)	(KBr) (hydrochloride) 2929. 2664. 2551. 1590. 1508. 1490. 1241. 1170. 872. 842. 749. 694	1.84-1.94(6H, m). 2.09(2H, m). 2.44-2.53(3H, m). 2.66(2H, t). 3.10(2H, m). 6.94(2H, dd). 6.99(2H, d). 7.07(1H, t). 7.17-7.21(5H, m). 7.26-7.33 (4H, m)	$C_{21}H_{24}ClNO$ (hydrochloride)· 1/5H_2O C 75.87 H 7.44 N 3.40 Calcd; 75.84 7.32 3.40 Found;
23		Colorless crystals (fumarate) 156-158°C (methanol/ ether)	(KBr) (fumarate) 2930. 2497. 1715. 1590. 1496. 1294. 1100. 983. 872. 797. 696	1.81-1.86(4H, m). 2.10-2.16 (2H, m). 2.50(1H, tt). 3.14(2H, m). 3.23(2H, m). 3.86(3H, s). 3.869(3H, s). 3.873(3H, s). 6.24(1H, dt). 6.66(1H, d). 6.74(1H, d). 6.94(2H, d). 7.00(2H, d). 7.07(1H, t). 7.18-7.34(5H, m)	$C_{21}H_{23}NO_5$ (fumarate)· 1/4H_2O C 68.32 H 6.52 N 2.41 Calcd; 68.25 6.45 2.42 Found;
24		Yellow crystals (hydrochloride) 98-100°C (methanol/ ether)	(KBr) (hydrochloride) 3424. 2932. 2586. 1654. 1594. 1511. 1484. 1280. 1172. 1125. 1032. 972. 868. 808. 756. 693	2.59(2H, d). 2.78(2H, t). 3.22(2H, d). 3.27(2H, d). 3.90(3H, s). 5.62(1H, brs). 6.03(1H, m). 6.19(1H, dt). 6.49(1H, d). 6.84-7.36(12H, m)	$C_{21}H_{23}ClNO_5$ (hydrochloride)· 3/2H_2O C 67.99 H 6.55 N 2.94 Calcd; 67.83 6.16 3.07 Found;

Compound no.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR (CDCl$_3$)	Elemental analysis
25		Colorless crystals (hydrochloride) 198-200°C (methanol/ ether)	(KBr) (hydrochloride) 3445. 2930. 2606. 1654. 1592. 1514. 1468. 1254. 1164. 984. 834. 747. 692	1.75-1.87(4H, m), 2.10(2H, dt), 2.50(1H, t), 3.12(2H, m), 3.19(2H, m), 6.24(1H, dt), 6.50(1H, d), 6.93-7.02(6H, m), 7.07(1H, t), 7.18(2H, d), 7.25-7.36(4H, m)	$C_{21}H_{23}ClFNO$ (hydrochloride)·(1/2)H_2O C H N Calcd: 72.13 6.52 3.24 Found: 72.22 6.38 3.36
26		Colorless crystals (fumarate) 158-160°C (methanol/ ether)	(KBr) (fumarate) 3034. 2944. 2532. 1718. 1596. 1511. 1260. 868. 754. 691	0.85(1H, ddd), 1.00(1H, ddd), 1.30(1H, m), 1.70(1H, m), 1.77-1.85(4H, m), 2.10-2.15 (2H, m), 2.42-2.51(2H, m), 2.56(1H, dd), 3.18(2H, m), 6.93(2H, d), 6.99(2H, d), 7.06-7.33(10H, m)	$C_{31}H_{33}NO_5$ (fumarate) C H N Calcd: 74.53 6.66 2.80 Found: 74.06 6.65 2.80
27		Colorless crystals (hydrochloride) 146-148°C (methanol/ ether)	(KBr) (hydrochloride) 2930. 1589. 1508. 1485. 1240. 1172. 978. 825	1.75-1.95(4H, m), 2.22(2H, td), 2.5(1H, m), 2.83(2H, t), 3.11(2H, d), 4.1(2H, t), 6.85(1H, d), 6.86(1H, d), 6.9(2H, d), 6.9-7.05(4H, m), 7.1(1H, t), 7.17(2H, d), 7.31(2H, t)	———
28		Colorless crystals (hydrochloride) 154-156°C (methanol/ ether)	(KBr) (hydrochloride) 2920. 2510. 1589. 1514. 1502. 1234. 1170. 1073. 870. 826. 761. 694	1.69-1.83(8H, m), 2.05(2H, t), 2.42-2.52(3H, m), 3.07(2H, m), 3.95(2H, t), 6.81-6.85(2H, m), 6.93-7.01(6H, m), 7.07(1H, t), 7.18(2H, d), 7.25-7.33(2H, m)	$C_{21}H_{23}ClFNO_2$ (hydrochloride) C H N Calcd: 71.12 6.86 2.98 Found: 70.90 6.80 3.09

Compound no.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR ($CDCl_3$)	Elemental analysis
29		Colorless crystals (hydrochloride) 178-180°C (methanol/ ether)	(KBr) (hydrochloride) 2944. 2481. 1590. 1490. 1287. 1238. 1170. 1103. 870. 802. 748. 693	1.70-1.82(4H, m). 2.10(2H, dt). 2.48(1H, tt). 3.02(2H, m). 3.52(2H, s). 3.86(3H, s). 3.88(3H, s). 3.90(3H, s). 6.65(1H, d). 6.92-7.09(6H, m). 7.18(2H, d). 7.28-7.33(2H, m)	$C_{27}H_{33}ClNO_4$ (hydrochloride)·H_2O C H N Calcd; 66.45 7.02 2.87 Found; 66.56 6.65 2.89
30		Colorless crystals (hydrochloride) 194-196°C (methanol/ ether)	(KBr) (hydrochloride) 2942. 2642. 2547. 1687. 1600. 1508. 1490. 1250. 1157. 832	1.66-1.75(2H, m). 1.81(2H, d). 1.99(2H, dt). 2.08(2H, t). 2.43-2.50(3H, m). 3.00(2H, t). 3.05(2H, d). 6.92-6.95(2H, m). 6.98-7.00(2H, m). 7.06-7.16 (5H, m). 7.29-7.34(2H, m). 7.99-8.04(2H, m)	$C_{27}H_{32}ClFNO_2$(hydrochloride) C H N Calcd; 71.43 6.44 3.09 Found; 71.01 6.37 3.09
31		Colorless crystals (hydrochloride) 195-197°C (methanol/ ether)	(KBr) (hydrochloride) 2930. 2666. 2448. 1599. 1511. 1502. 1451. 1218. 978. 941. 847. 803. 742. 693	2.58(2H, d). 2.76(2H, t). 3.21(2H, m). 3.29(2H, d). 3.92(2H, s). 6.04(1H, m). 6.35(1H, dt). 6.57(1H, d). 6.96(2H, t). 7.09-7.40(12H, m)	$C_{27}H_{31}ClFN$ (hydrochloride)·$1/5H_2O$ C H N Calcd; 76.56 6.52 3.31 Found; 76.62 6.43 3.32
32		Colorless crystals (hydrochloride) 203-205°C (methanol/ ether)	(KBr) (hydrochloride) 2940. 2488. 1600. 1504. 1458. 1221. 1158. 978. 810. 752. 695	1.78-1.84(4H, m). 2.09(2H, dt). 2.47(1H, tt). 3.11(2H, m). 3.19(2H, dd). 3.91(2H, s). 6.33(1H, dt). 6.53(1H, d). 6.93-6.98(2H, m). 7.07-7.40(11H, m)	$C_{27}H_{31}ClFN$ (hydrochloride) C H N Calcd; 76.85 6.93 3.32 Found; 76.76 6.86 3.33

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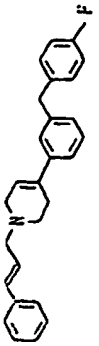
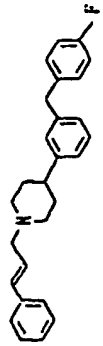
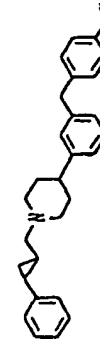
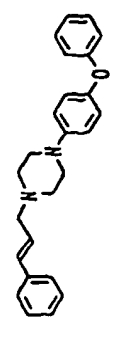
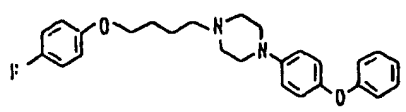
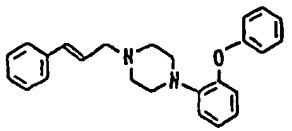
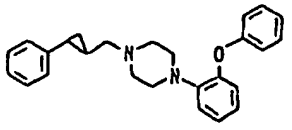
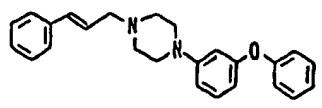
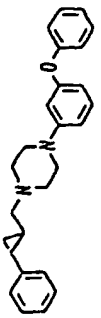
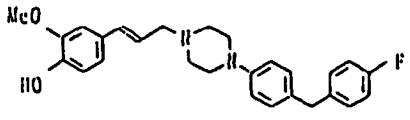
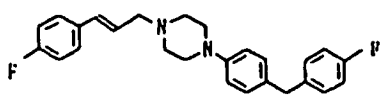
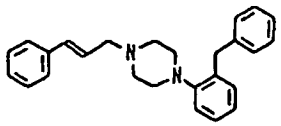
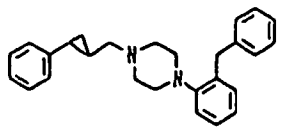
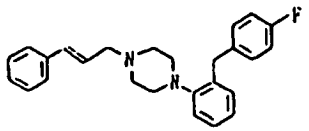
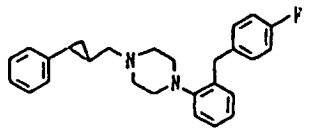
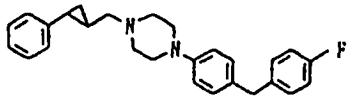
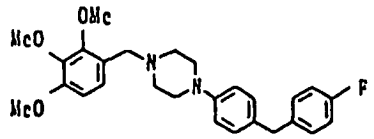
Compound no.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR ($CDCl_3$)	Elemental analysis
33		Colorless crystals (hydrochloride) 176-178°C (methanol/ ether)	(KBr) (hydrochloride) 2929. 2500. 1604. 1512. 1504. 1457. 1222. 1158. 820. 755. 700	0.85(1H, ddd). 0.97(1H, ddd). 1.29(1H, m). 1.70(1H, m). 1.81(4H, m). 2.12(2H, m). 2.44(2H, m). 2.52(1H, m). 3.17(2H, m). 3.91(2H, s). 6.96(1H, t). 7.05-7.15(7H, m). 7.23-7.27(3H, m)	$C_{18}H_{19}ClFN$ (hydrochloride)·1/4H_2O C H N Calcd: 76.34 7.21 3.18 Found: 76.28 7.10 3.24
34		Colorless crystals (hydrochloride) 160-162°C (methanol/ ether)	(KBr) (hydrochloride) 3498. 2908. 2500. 1654. 1508. 1448. 1226. 1156. 973	2.35(2H, m). 2.75(2H, t). 3.2(2H, m). 3.35(2H, d). 4.00(2H, s). 5.52(1H, m). 6.41(1H, dt). 6.61(1H, d). 6.9-7.6(13H, m)	$C_{17}H_{17}ClFN$ (hydrochloride) C H N Calcd; 77.22 6.48 3.34 Found; 76.98 6.47 3.34
35		Colorless crystals (hydrochloride) 200-202°C (methanol/ ether)	(KBr) (hydrochloride) 3436. 2942. 2530. 1602. 1508. 1450. 1436. 1220. 1158. 978	1.7-2.1(4H, m). 2.75(1H, m). 3.07(2H, m). 3.16(2H, d). 3.4(2H, m). 4.05(2H, s). 6.25(1H, d). 6.56(1H, d). 6.8-7.5(13H, m)	$C_{17}H_{18}ClFN$ (hydrochloride) C H N Calcd; 76.85 6.93 3.32 Found; 76.45 6.93 3.28
36		Colorless foam (hydrochloride)	(KBr) (hydrochloride) 3388. 3030. 2935. 2656. 2524. 1604. 1508. 1456. 1220. 957	0.85(1H, dt). 0.97(1H, dt). 1.27(1H, m). 1.47-1.66(4H, m). 1.67(1H, m). 1.7-2.04(2H, m). 2.4(1H, dd). 2.52(1H, dd). 2.66(1H, m). 3.1(2H, m). 4.02(1H, s). 6.85-7.35(13H, m)	———

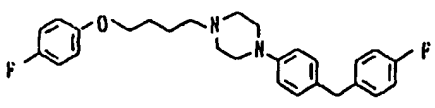
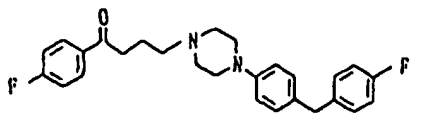
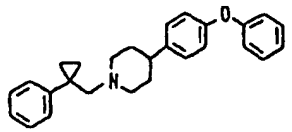
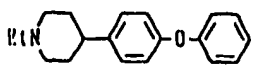
Compound no.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR ($CDCl_3$)	Elemental analysis
37		A colorless oil (hydrochloride)	(KBr) (hydrochloride) 2944. 2512. 1607. 1508. 1451. 1216. 1094. 989	2.6(2H, m). 2.78(2H, t). 3.2-3.4(4H, m). 3.97(2H, s). 6.06(1H, brs). 6.35(1H, dt). 6.59(1H, d). 6.9-7.5(8H, m)	———
38		Colorless crystals (hydrochloride) 190-192°C (methanol/ ether)	(KBr) (hydrochloride) 2944. 2512. 1607. 1508. 1451. 1216. 1158. 989	1.8(4H, m). 2.07(2H, m). 2.47(1H, m). 3.1(2H, m). 3.29(2H, d). 3.91(2H, s). 6.33(1H, dt). 6.53(1H, d). 6.9-7.5(13H, m)	$C_{31}H_{32}ClFN$ (hydrochloride) C 76.85 H 6.93 N 3.32 Calcd: 76.77 6.88 3.34 Found:
39		Colorless foam (hydrochloride)	(KBr) (hydrochloride) 3446. 2940. 2658. 2526. 1604. 1508. 1436. 1219. 1157. 1094	0.87(1H, dt). 1.0(1H, dt). 1.31(1H, m). 1.72(1H, m). 1.84(4H, m). 2.25(2H, m). 2.43(1H, dd). 2.47(1H, m). 2.52(1H, dd). 3.2(2H, m). 3.94(2H, s). 6.9-7.4(13H, m)	———
40		Colorless crystals (dihydrochloride) 205-207°C (methanol/ ether)	(KBr) (dihydrochloride) 2402. 1590. 1510. 1490. 1456. 1250. 1171. 960. 750. 693	2.69(4H, m). 3.20(4H, m). 3.23(2H, d). 6.31(1H, dt). 6.57(1H, d). 6.90-7.04(7H, m). 7.23-7.33(5H, m). 7.39(2H, d)	$C_{31}H_{31}Cl_2NO$ (hydrochloride)·2/5H_2O C 66.64 H 6.44 N 6.22 Calcd: 66.66 6.14 6.24 Found:

Compound no.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR ($CDCl_3$)	Elemental analysis
41		Colorless crystals (dihydrochloride) 173-175°C (methanol/ ether)	(KBr) (dihydrochloride) 2984. 2354. 1588. 1504. 1490. 1456. 1250. 1208. 829. 756	1.71(2H. t). 1.82(2H. t). 2.47(2H. t). 2.62(4H. t). 3.16(4H. t). 3.96(2H. t). 6.82(1H. d). 6.83(1H. d). 6.90-6.98(8H. m). 7.02(1H. t). 7.26(1H. d). 7.29(1H. d)	$C_{31}H_{31}Cl_2FN_2O_2$ (hydrochloride) C: Calcd: 63.29, Found: 63.12; H: Calcd: 6.33, Found: 6.22; N: Calcd: 5.68, Found: 5.68
42		Colorless crystals (dihydrochloride) 140-142°C (methanol/ ether)	(KBr) (dihydrochloride) 2960. 2380. 1590. 1494. 1446. 1235. 1171. 978. 951. 750	2.49(4H. m). 3.13(2H. d). 3.14(4H. t). 6.25(1H. dt). 6.49(1H. d). 6.91-6.98(4H. m). 7.03(2H. t). 7.08-7.12(1H. m). 7.21-7.31(5H. m). 7.36(2H. d)	$C_{31}H_{32}Cl_2N_2O$ (hydrochloride)·$1/4H_2O$ C: Calcd: 67.04, Found: 67.01; H: Calcd: 6.41, Found: 6.28; N: Calcd: 6.25, Found: 6.26
43		Colorless crystals (dihydrochloride) 123-125°C (methanol/ ether)	(KBr) (dihydrochloride) 3012. 2360. 1588. 1492. 1448. 1256. 1202. 969. 750. 694	0.80(1H. ddd). 0.93(1H. ddd). 1.22(1H. m). 1.65(1H. m). 2.32(1H. dd). 2.47(1H. dd). 2.51(4H. m). 3.12(4H. t). 6.90-7.15(10H. m). 7.22-7.28 (4H. m)	$C_{31}H_{32}Cl_2N_2O$ (hydrochloride)·$1/5H_2O$ C: Calcd: 67.73, Found: 67.79; H: Calcd: 6.65, Found: 6.50; N: Calcd: 6.08, Found: 6.12
44		Colorless crystals (dihydrochloride) 148-150°C (methanol/ ether)	(KBr) (dihydrochloride) 2375. 1591. 1488. 1260. 1210. 980. 949. 778. 753. 688	2.64(4H. t). 3.21(2H. d). 3.22(4H. t). 6.29(1H. dt). 6.46(1H. dd). 6.55(1H. d). 6.61(1H. t). 6.67(1H. dd). 7.01(1H. d). 7.07(1H. t). 7.16-7.25(5H. m). 7.31(2H. t). 7.39(2H. d)	$C_{31}H_{32}Cl_2N_2O$ (hydrochloride)·$1/4H_2O$ C: Calcd: 67.04, Found: 66.92; H: Calcd: 6.41, Found: 6.31; N: Calcd: 6.25, Found: 6.25

Compound no.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR ($CDCl_3$)	Elemental analysis
45		Colorless crystals (dihydrochloride) 172-174°C (methanol/ether)	(KBr) (dihydrochloride) 2530. 2346. 1580. 1515. 1485. 1220. 954. 748. 698	0.85(1H, ddd), 0.98(1H, ddd). 1.26(1H, m), 1.70(1H, m). 2.39(1H, dd), 2.59(1H, dd). 2.66(4H, m), 3.19(4H, t). 6.45(1H, dd), 6.59(1H, s). 6.65(1H, d), 6.99-7.33(11H, m)	———
46		Colorless crystals (dihydrochloride) 166-169°C (methanol/ether)	(KBr) (dihydrochloride) 2987. 2438. 1661. 1491. 1421. 1292. 1236. 1201. 1096. 871. 754	2.64(4H, t), 3.15(4H, t). 3.54(2H, s), 3.86(3H, s). 3.88(3H, s), 3.90(3H, s). 6.66(1H, d), 6.91-6.96(5H, m). 7.00-7.04(2H, m), 7.26-7.30 (2H, m)	$C_{31}H_{34}Cl_2N_2O_4$(hydrochloride) C H N Calcd: 61.30 6.73 5.50 Found: 61.22 6.25 5.51
47		Colorless crystals (dihydrochloride) 180-182°C (methanol/ether)	(KBr) (dihydrochloride) 2370. 1603. 1508. 1458. 1223. 966. 820. 754. 695	2.66(4H, t), 3.19(4H, t). 3.21(2H, d), 3.86(2H, s). 6.30(1H, dt), 6.55(1H, d). 6.86(2H, d), 6.94(2H, t). 7.05(2H, d), 7.11(2H, dd). 7.23(1H, t), 7.31(2H, t). 7.38(2H, d)	$C_{31}H_{32}Cl_2FN$(hydrochloride) C H N Calcd: 67.97 6.36 6.10 Found: 67.80 6.27 6.10
48		Colorless crystals (dihydrochloride) 168-170°C (methanol/ether)	(KBr) (dihydrochloride) 2934. 2365. 1597. 1510. 1494. 1460. 1418. 1298. 1222. 1098. 1060. 1016. 948. 813	2.66(4H, t), 3.19(4H, t). 3.22(2H, d), 3.86(3H, s). 3.866(5H, s), 3.871(3H, s). 6.20(1H, dt), 6.66(1H, d). 6.75(1H, d), 6.86(2H, d). 6.94(2H, t), 7.05(2H, d). 7.11(2H, dd), 7.18(1H, d)	$C_{31}H_{34}Cl_2FN_2O_3$(hydrochloride) C H N Calcd: 63.40 6.42 5.10 Found: 63.75 6.39 5.23

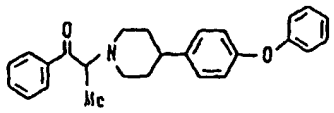
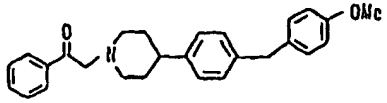
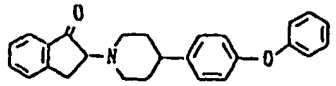
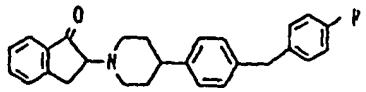
Compound no.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR (CDCl$_3$)	Elemental analysis
49		Yellow crystals (dihydrochloride) 115-117°C (methanol/ ether)	(KBr) (dihydrochloride) 3134. 2544. 1602. 1514. 1456. 1279. 1220. 1159. 1122. 1032. 808	2.66(4H. t). 3.19(2H. d). 3.20(4H. t). 3.86(2H. s). 3.89(3H. s). 5.67(1H. brs). 6.14(1H. dt). 6.47(1H. d). 6.84-6.88(4H. m). 6.94(3H. m). 7.05(2H. d). 7.11(2H. dd)	———
50		Colorless crystals (dihydrochloride) 148-150°C (methanol/ ether)	(KBr) (dihydrochloride) 2364. 1602. 1510. 1436. 1228. 1158. 962. 830	2.65(4H. t). 3.19(4H. t). 3.20(2H. d). 3.86(2H. s). 6.21(1H. dt). 6.51(1H. d). 6.86(2H. dd). 6.92-7.13 (10H. m). 7.34(2H. dd)	$C_{31}H_{32}Cl_2F_2N_2$ (hydrochloride) C H N Calcd: 65.41 5.91 5.87 Found: 65.52 5.81 5.87
51		Colorless crystals (dihydrochloride) 145-147°C (methanol/ ether)	(KBr) (dihydrochloride) 3028. 2939. 1598. 1494. 1449. 1367. 1239. 1169. 1070. 1029. 964. 744. 700	2.63(4H. m). 2.92(4H. t). 3.22(2H. d). 4.08(2H. s). 6.31(1H. dt). 6.55(1H. d). 7.02(1H. dd). 7.10(1H. d). 7.16-7.29(8H. m). 7.31(2H. d). 7.38(2H. d)	———
52		Colorless crystals (dihydrochloride) 93-95°C (methanol/ ether)	(KBr) (dihydrochloride) 3354. 2957. 2468. 1604. 1496. 1463. 1226. 1087. 1030. 972. 940. 761. 697	0.86(1H. ddd). 0.98(1H. ddd). 1.28(1H. m). 1.70(1H. m). 2.43(1H. dd). 2.56(1H. dd). 2.66(4H. m). 2.90(4H. t). 4.07(2H. s). 6.99-7.27(14H. m)	$C_{31}H_{32}Cl_2N_2$ (hydrochloride) C H N Calcd: 71.20 7.08 6.15 Found: 70.77 7.16 6.19

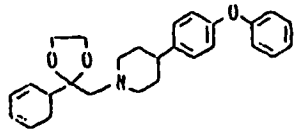
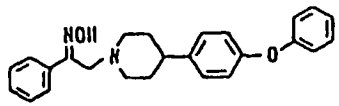
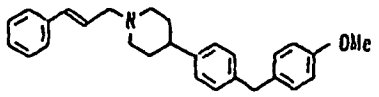
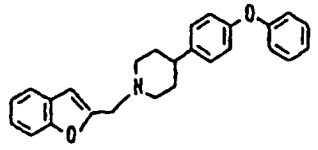
Compound no.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR (CDCl$_3$)	Elemental analysis
53		Colorless crystals (dihydrochloride; 136-138°C (methanol/ ether)	(KBr) (dihydrochloride) 3416. 2921. 2360. 1600. 1509. 1493. 1451. 1222. 1158. 968. 768. 744. 692	2.63(4H, m). 2.90(4H, m). 3.22(2H, d). 4.03(2H, s). 6.31(1H, dt). 6.55(1H, d). 6.94(2H, dt). 7.01-7.21 (2H, m). 7.23-7.26(5H, m). 7.31(2H, t). 7.39(2H, d)	———
54		Colorless crystals (dihydrochloride; 108-110°C (methanol/ ether)	(KBr) (dihydrochloride) 3416. 2921. 2580. 1601. 1508. 1456. 1224. 1158. 764. 700	0.85(1H, ddd). 0.98(1H, ddd). 1.28(1H, m). 1.70(1H, m). 2.43(1H, dd). 2.58(1H, dd). 2.65(4H, m). 2.89(4H, t). 4.02(2H, s). 6.92(2H, t). 7.03(2H, dd). 7.06(2H, d). 7.11-7.27(7H, m)	$C_{27}H_{29}Cl_2FN_2$ (hydrochloride) C H N Calcd: 68.50 6.60 5.92 Found: 69.00 6.50 6.03
55		Colorless crystals (fumarate); °C 160-162°C (methanol/ ether)	(KBr) (fumarate) 3011. 2830. 2570. 1714. 1576. 1558. 1513. 1436. 1225. 1157. 977. 811. 758. 697	0.85(1H, ddd). 0.98(1H, ddd). 1.27(1H, m). 1.70(1H, m). 2.40(1H, dd). 2.60(1H, dd). 2.69(4H, ddd). 3.17(4H, t). 3.86(2H, s). 6.85(2H, d). 6.94(2H, t). 7.05(4H, t). 7.09-7.16(3H, m). 7.25(2H, t)	$C_{31}H_{31}FN_2O_4$ (fumarate)·3/5H_2O C H N Calcd: 70.60 6.54 5.31 Found: 70.67 6.35 5.33
56		Colorless crystals (dihydrochloride; 192-194°C (methanol/ ether)	(KBr) (dihydrochloride) 3420. 2943. 2358. 1602. 1504. 1288. 1158. 1106. 959. 812	2.62(4H, t). 3.15(4H, t). 3.53(2H, s). 3.86(3H, s). 3.88(5H, s). 3.89(3H, s). 6.65(1H, d). 6.84(2H, d). 6.90-7.08(5H, m). 7.11(2H, dd)	$C_{31}H_{37}Cl_2FN_2O_4$(hydrochloride)·1/2H_2O C H N Calcd: 60.90 6.44 5.20 Found: 60.71 6.13 5.27

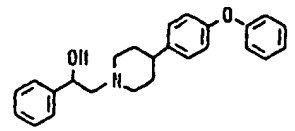
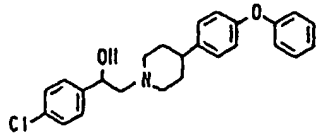
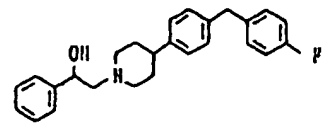
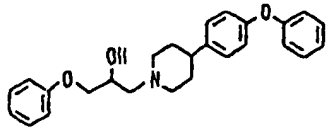
Compound no.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR ($CDCl_3$)	Elemental analysis
57		Colorless crystals (dihydrochloride) 135-137°C (methanol/ ether)	(KBr) (dihydrochloride) 2987. 2338. 1602. 1511. 1505. 1475. 1458. 1248. 1222. 836. 757	1.63-1.87(4H, m). 2.45(2H, t). 2.60(4H, t). 3.17(4H, t). 3.87(2H, s). 3.95(2H, t). 6.81-6.88(4H, m). 6.96(4H, dt). 7.04-7.15(4H, m)	$C_{21}H_{21}Cl_2F_2N_2O$ (hydrochloride) C: Calcd: 63.65, Found: 63.89; H: Calcd: 6.33, Found: 6.27; N: Calcd: 5.50, Found: 5.55
58		Colorless crystals (dihydrochloride) 159-161°C (methanol/ ether)	(KBr) (dihydrochloride) 2987. 2337. 1688. 1598. 1511. 1503. 1437. 1214. 1157. 991. 819	1.98(2H, m). 2.46(2H, t). 2.58(4H, t). 3.00(2H, t). 3.11(4H, t). 3.86(2H, s). 6.83(2H, d). 6.94(2H, t). 7.04(2H, d). 7.11(2H, d). 7.13(2H, d). 7.99(2H, d). 8.01(2H, d)	———
59		Colorless crystals (hydrochloride) 181-182°C (ether/ methylene chloride)	(KBr) (hydrochloride) 3428. 3028. 2927. 2638. 2544. 1589. 1508. 1490. 1433. 1239. 1166. 966	0.79(2H, dd). 0.95(2H, dd). 1.55-1.85(4H, m). 2.12(2H, td). 2.43(1H, tt). 2.62(2H, s). 3.1(2H, m). 6.9-7.5(14H, m)	$C_{21}H_{18}ClNO$ (hydrochloride) C: Calcd: 77.21, Found: 76.89; H: Calcd: 7.20, Found: 7.19; N: 3.34
60		Colorless crystals (hydrochloride) 148-150°C (methanol/ ether)	($CHCl_3$) 3019. 2399. 2360. 1634. 1510. 1488. 1418. 930. 870	1.54(3H, t). 2.06-2.09(2H, m). 2.65(2H, m). 2.79-2.82(3H, m). 3.09(2H, q). 3.64-3.60(2H, m). 6.96-7.35(9H, m)	———

Compound no.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR (CDCl$_3$)	Elemental analysis
61		Colorless crystals (dihydrochloride) 133-135°C (methanol/ ether)	(CHCl$_3$) 2943. 2364. 1614. 1509. 1456. 1378. 1290. 1156. 1007. 924. 816	2.34(3H, s). 2.56(4H, t). 3.17(4H, t). 3.86(2H, s). 6.86(2H, d). 6.92-6.99(2H, m). 7.05(2H, d). 7.10-7.13(2H, m)	$C_{19}H_{21}Cl_2FN_2$(hydrochloride)·5/4H_2O C H N Calcd: 60.51 6.49 7.84 Found: 57.02 6.49 7.37
62		Colorless crystals (hydrochloride) 180-190°C (methylene chloride/ ether)	(KBr) (hydrochloride) 3428. 2930. 2546. 1602. 1508. 1436. 1222. 1155. 968. 813. 759. 701	0.74(2H, dd). 0.87(2H, dd). 1.60-1.71(4H, m). 2.00(2H, dt). 2.38(1H, t). 2.59(2H, s). 3.07(2H, d). 3.90(2H, s). 7.05-7.38(13H, m)	$C_{27}H_{27}ClFN$ (hydrochloride)·1/5H_2O C H N Calcd: 76.50 7.20 3.19 Found: 76.64 7.37 3.17
63		Colorless crystals (hydrochloride) 179-181°C (methanol/ ether)	(KBr) (hydrochloride) 3402. 2928. 2620. 2544. 1694. 1599. 1508. 1450. 1225. 962. 755. 690	1.81-1.96(4H, m). 2.30(2H, dt). 2.51(1H, t). 3.14(2H, m). 3.88(2H, s). 3.92(2H, m). 6.94-8.03(13H, m)	$C_{28}H_{29}ClFNO$ (hydrochloride)·1/5H_2O C H N Calcd: 72.64 6.49 3.26 Found: 72.52 6.35 3.30
64		Colorless crystals (hydrochloride) 183-185°C (methanol/ ether)	(KBr) (hydrochloride) 3391. 2948. 2537. 1703. 1590. 1508. 1490. 1450. 1248. 755. 691	1.82-1.95(4H, m). 2.30(2H, dt). 2.52(1H, t). 3.13(2H, m). 3.85(2H, s). 6.94(2H, dd). 7.00(2H, d). 7.08(1H, t). 7.19(2H, d). 7.32(2H, m). 7.47(2H, t). 7.57(1H, t). 8.03(2H, d)	$C_{28}H_{29}ClNO_2$(hydrochloride)·1/4H_2O C H N Calcd: 72.80 6.48 3.40 Found: 72.75 6.36 3.43

Compound no.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR ($CDCl_3$)	Elemental analysis
65		Colorless crystals (hydrochloride) 223-225°C (methanol/ ether)	(KBr) (hydrochloride) 2931. 2528. 1601. 1508. 1445. 1220. 1157. 969. 819. 748. 694	1.80-1.83(4H, m). 2.10(2H, dt). 2.42-2.55(5H, m). 3.09(2H, m). 3.91(2H, s). 6.20-6.26(1H, m). 6.44(1H, m). 6.94-7.30(13H, m)	$C_{31}H_{31}ClFN$ (hydrochloride)·1/5H_2O C H N Calcd: 76.50 7.20 3.19 Found: 76.70 7.11 3.21
66		Colorless crystals (hydrochloride) 196-198°C (methanol/ ether)	(KBr) (hydrochloride) 3444. 2936. 1681. 1601. 1508. 1490. 1237. 1173. 964. 832	1.82-1.99(4H, m). 2.32(2H, dt). 2.52(1H, tt). 3.13(2H, m). 3.80(2H, s). 3.87(3H, s). 6.94(4H, d). 6.99(2H, dd). 7.07(1H, t). 7.19(2H, dd). 7.31(2H, t). 8.04(2H, dd)	$C_{31}H_{31}ClNO_3$ (hydrochloride) C H N Calcd: 71.30 6.44 3.20 Found: 70.72 6.61 3.18
67		Colorless crystals (hydrochloride) 185-186°C (methanol/ ether)	(KBr) (hydrochloride) 3484. 2930. 2646. 1692. 1600. 1510. 1492. 1250. 1237. 760	1.82-1.84(4H, m). 2.29(2H, dt). 2.51(1H, tt). 3.09(2H, m). 3.78(2H, s). 6.94(2H, dd). 6.99(2H, d). 7.07(1H, t). 7.12(2H, d). 7.17(2H, t). 7.31(2H, dt). 8.10(2H, dd)	$C_{31}H_{31}ClFNO_3$ (hydrochloride) C H N Calcd: 70.50 5.92 3.29 Found: 70.22 5.88 3.29
68		Colorless crystals (hydrochloride) 173-176°C (methanol/ ether)	(KBr) (hydrochloride) 3418. 2946. 1694. 1590. 1510. 1488. 1403. 1242. 962. 871	1.79-1.87(4H, m). 2.28(2H, dt). 2.53(1H, tt). 3.07(2H, m). 3.77(2H, s). 6.94(2H, d). 6.99(2H, d). 7.06(1H, t). 7.16(2H, d). 7.24(2H, t). 7.42(2H, d). 7.99(2H, d)	$C_{31}H_{31}Cl_2NO_3$ (hydrochloride) C H N Calcd: 67.88 5.70 3.17 Found: 67.59 5.62 3.13

Compound no.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR ($CDCl_3$)	Elemental analysis
69		Colorless crystals (hydrochloride) 202-204°C (methanol/ ether)	(KBr) (hydrochloride) 3444. 2937. 1686. 1590. 1508. 1490. 1449. 1235. 978. 704	1.31(3H, d). 1.65(1H, dt). 1.76(2H, dt). 1.85(1H, m). 2.29(1H, d). 2.46(1H, tt). 2.67(1H, dt). 2.89(1H, m). 3.07(1H, m). 4.15(1H, q). 6.92(2H, dd). 6.98(2H, d). 7.06(1H, t). 7.14(2H, d). 7.28(2H, t). 7.45(2H, t). 7.55(1H, t). 8.12(2H, d)	$C_{19}H_{21}ClNO_2$ (hydrochloride) C H N Calcd: 74.01 6.69 3.32 Found: 74.12 6.87 3.31
70		Colorless crystals (hydrochloride) 210-212°C (methanol/ ether)	(KBr) (hydrochloride) 3442. 2935. 2649. 1699. 1511. 1450. 1245. 1031. 810. 759. 690	1.79-1.93(4H, m). 2.28(2H, dt). 2.48(1H, tt). 3.11(2H, m). 3.77(3H, s). 3.83(2H, s). 3.88(2H, s). 6.82(2H, d). 7.08-7.15(6H, m). 7.45(2H, t). 7.56(1H, t). 8.03(2H, d)	$C_{21}H_{25}ClNO_2$ (hydrochloride) C H N Calcd: 74.38 6.94 3.21 Found: 74.19 6.93 3.18
71		Colorless crystals (hydrochloride) 166-167°C (methanol/ ether)	(KBr) (hydrochloride) 3464. 2608. 1721. 1608. 1588. 1511. 1484. 1236. 907	1.83-1.89(4H, m). 2.47-2.56 (2H, m). 2.80-2.88(1H, m). 2.92(1H, m). 3.03(1H, m). 3.19(1H, dd). 3.30(1H, dd). 3.38(1H, dd). 6.94(2H, d). 6.99(2H, d). 7.07(1H, t). 7.18(2H, d). 7.31(2H, t). 7.38(1H, t). 7.46(1H, d). 7.61(1H, t). 7.77(1H, d)	$C_{21}H_{23}ClNO_2$ (hydrochloride) C H N Calcd: 74.36 6.24 3.34 Found: 74.10 6.22 3.35
72		Pale yellow crystals (hydrochloride) 175-177°C (methanol/ ether)	(KBr) (hydrochloride) 3476. 2925. 1720. 1607. 1508. 1467. 1221. 1158. 811. 761	1.80-1.88(4H, m). 2.50(2H, dt). 2.81(1H, m). 2.89(1H, m). 3.02(1H, m). 3.18(1H, dd). 3.29(1H, dd). 3.77(1H, dd). 3.91(2H, s). 6.95(2H, t). 7.07-7.16(6H, m). 7.37(1H, t). 7.46(1H, d). 7.60(1H, t). 7.76(1H, d)	———

Compound no.	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR ($CDCl_3$)	Elemental analysis
73		Colorless crystals (fumarate) 199-200°C (methanol/ ether)	(KBr) (fumarate) 3450. 2960. 2900. 1686. 1560. 1508. 1490. 1234. 1214. 1026. 707	1.69-1.74(4H. m). 2.27(2H. m). 2.41(1H. m). 2.81(2H. s). 3.03(2H. m). 3.84(2H. m). 4.13(2H. m). 6.9-7.45(10H. m). 7.17(2H. d). 7.54(2H. d)	$C_{31}H_{31}NO_7$ (fumarate) C H N Calcd: 70.04 6.26 2.63 Found: 69.46 6.29 2.64
74		Foamy substance (hydrochloride)	(KBr) (hydrochloride) 3416. 3060. 1589. 1508. 1489. 1238. 1170. 870. 752. 696	1.55-2.10(4H. m). 2.19 and 2.32 (total 2H. both m). 2.54 and 2.58(total 1H. both t). 3.09 and 3.23 (total 2H. both m). 3.43 and 3.85 (total 2H. both s). 6.90-8.80 (15H. m)	———
75		Colorless crystals (hydrochloride) 211-212°C (methanol/ ether)	(KBr) (hydrochloride) 3451. 2928. 2639. 1512. 1451. 1247. 1178. 1032. 749. 694	1.75-1.83(4H. m). 2.08(2H. dt) 2.47(1H. t). 3.10(2H. m). 3.19(2H. dd). 3.77(3H. s). 3.88(2H. s). 6.32(1H. dt). 6.53(1H. d). 6.82(2H. dd). 7.02-7.20(6H. m). 7.21(1H. t). 7.30(2H. t). 7.38(2H. d)	$C_{25}H_{25}ClNO$ (hydrochloride) C H N Calcd: 77.49 7.43 3.23 Found: 77.69 7.73 3.21
76		Colorless crystals (hydrochloride) 212-214°C (methanol/ ether)	(KBr) (hydrochloride) 3444. 2928. 2521. 1589. 1508. 1490. 1453. 1241. 1170. 870. 754. 674	1.82-1.89(4H. m). 2.21(2H. dt). 2.48(1H. t). 3.10(2H. m). 3.74(2H. s). 6.60(1H. s). 6.93(2H. d). 6.99(2H. d). 7.07(1H. t). 7.16-7.33(6H. m). 7.50(1H. d). 7.51(1H. d)	$C_{24}H_{24}ClNO_2$ (hydrochloride) C H N Calcd: 74.36 6.24 3.34 Found: 74.46 6.27 3.37

Compound no	Chemical structure	Properties m.p. (recrystallization solvent)	IR	^{1}H-NMR ($CDCl_3$)	Elemental analysis
77		Colorless crystals (hydrochloride) 196-197°C (methanol/ ether)	(KBr) (hydrochloride) 3302. 2962. 2692. 2362. 1590. 1508. 1490. 1244. 1061. 870. 754. 694	1.75-2.05(4H, m). 2.23(1H, m). 2.40-2.70(4H, m). 2.98(1H, m). 3.33(1H, m). 4.79(1H, dd). 6.90-7.50(14H, m)	$C_{21}H_{21}ClNO_2$ (hydrochloride) C H N Calcd: 73.25 6.88 3.42 Found: 72.99 6.76 3.41
78		Colorless crystals (hydrochloride) 215-216°C (methanol/ ether)	(KBr) (hydrochloride) 3220. 2949. 2639. 1590. 1509. 1490. 1243. 1074. 1016. 872. 819. 758	1.72-2.00(4H, m). 2.20(1H, m). 2.39-2.64(4H, m). 2.95(1H, m). 3.28(1H, m). 4.75(1H, dd). 6.98(2H, d). 7.02(2H, d). 7.11(1H, t). 7.21(2H, d). 7.35(6H, m)	$C_{21}H_{20}Cl_2NO_2$ (hydrochloride) C H N Calcd: 67.57 6.12 3.15 Found: 67.53 6.16 3.14
79		Colorless crystals (hydrochloride) 134-135°C (methanol/ ether)	(KBr) (hydrochloride) 3064. 1599. 1504. 1438. 1218. 1155. 962. 813. 761. 702	1.70-2.00(4H, m). 2.19(1H, m). 2.42-2.61(4H, m). 2.95(1H, m). 3.32(1H, m). 3.95(2H, s). 4.78(1H, dd). 7.14(2H, t). 7.16-7.52(11H, m)	$C_{21}H_{20}ClFNO$ (hydrochloride) C H N Calcd: 73.31 6.86 3.29 Found: 72.61 6.73 3.21
80		Colorless crystals (hydrochloride) 151-152°C (methanol/ ether)	(KBr) (hydrochloride) 3268. 2657. 1590. 1509. 1490. 1246. 1171. 1050. 755. 693	1.65-1.95(4H, m). 2.14(1H, m). 2.43(1H, m). 2.45-2.70(3H, m). 2.98(1H, m). 3.14(1H, m). 4.01(2H, m). 4.12(1H, m). 6.92-6.99 (5H, m). 7.01(2H, d). 7.08(1H, t). 7.18(2H, d). 7.25-7.40(4H, m)	$C_{21}H_{21}ClNO_3$ (hydrochloride) C H N Calcd: 70.98 6.87 3.18 Found: 70.90 6.82 3.20

Compound no.	Chemical structure	Properties m.p. (recrystallisation solvent)	IR	^{1}H-NMR ($CDCl_3$)	Elemental analysis
81		Colorless crystals (hydrochloride) 160-161°C (methanol/ ether)	(KBr) (hydrochloride) 3306. 2930. 2646. 1599. 1508. 1250. 1222. 812. 762. 694	1.70-2.00(4H, m). 2.16(1H, m). 2.40-2.76(4H, m). 3.01(1H, m). 3.15(1H, m). 3.95(1H, s). 4.03(2H, m). 4.13(1H, m). 6.90-7.40(13H, m)	$C_{17}H_{17}ClFNO$ (hydrochloride) C 71.12 H 6.85 N 3.07 Calcd; Found; 71.02 6.78 3.16
82		Colorless crystals (dihydrochloride) 130-131°C (methanol/ ether)	(KBr) (dihydrochloride) 2905. 2368. 1703. 1600. 1508. 1448. 1278. 1232. 968. 758. 688	2.79(4H, t). 3.26(4H, t). 3.89(4H, s). 6.88(2H, d). 6.97(2H, t). 7.10(2H, d). 7.15(2H, t). 7.49(2H, t). 7.60(1H, t). 8.05(2H, d)	$C_{21}H_{21}Cl_2FN_2O$ (hydrochloride) C 65.08 H 5.90 N 6.07 Calcd; Found; 65.72 5.95 6.16

[0195] The anti-veratrizine action of the above synthetic compounds, the T-type Ca^{2+} channel inhibiting action, the anti-convulsant action, the dopamine D_2 receptor blocking action, and the LD_{50} were evaluated by the following methods. The results are shown in Table 2, Table 3, Table 4, Table 5, and Table 6.

Veratridine-induced sodium channel activity inhibiting action

[0196] The membrane potential of the synaptosomes prepared from the brain membrane of Wistar rats (male, 10 to 12 weeks old) was measured by the method of Aiuchi et al. [T. Aiuchi et al: Biochimi. Biophys. Acta. 771, 228 (19854)] using a membrane potential sensitive fluorescent dye Rhodamine 6G to evaluate the effects of suppression of the compound on the veratridine-inducing depolarization response.

[0197] The results are shown in Table 2.

Table 2

Compound no.	Antiveratridine action (inhibiting rate %) (0.1 μm of compound)
18	16
19	26.1
21	20.3
26	36.5
28	38
29	9.9
32	33.3
41	20.8
46	11.7
47	22.9
48	20.5
49	17.3
56	18.4
57	25
58	33.9
62	23.9
63	31.1
64	34.5
65	38.7
66	19.6
67	15
68	38.9
69	11.2
73	16.1
74	14.6
75	55.2
77	31.1
78	44.4
79	37.1
80	49.7

Table 2 (continued)

Compound no.	Antiveratridine action (inhibiting rate %) (0.1 μm of compound)
81	24.1
82	16.9

T-Type Calcium Channel Inhibiting Action

[0198] The hippocampal CA1 pyramidal cells were isolated from Wistar rats (female, 1 week old) in accordance with the method of Takahashi et al. [K. Takahashi et al.; J. Pharmacol. Exp. Ther., 256, 169 (1991)] and the T-type calcium current under conditions of a fixed membrane potential was measured using the whole-cell configuration of the pach clamp technique. The effects of the compounds were evaluated from the rate of suppression of the peak current after one minute of application using the concentration clamp method.

[0199] The results are shown in Table 3.

Table 3

Compound no.	T-type Ca^{2+} channel inhibiting action IC_{50} (μM)
21	0.8
26	2.8
32	0.6
47	2.7
50	4.2
73	4.6
75	1.4
79	3.1
80	1.9

Audiogenic Seizure Suppressing Action

[0200] The audiogenic seizure suppressing action of the compounds was evaluated by the method of Sarro et al. [G. B. De Sarro et al.; Br. J. Pharmacol., 93, 247 (1988)]. That is, DBA/2N mice (male, 3 weeks) were administered with the compound dissolved in 10% 2-hydroxypropyl-β-cyclodextrin intraperitoneally. After 20 minutes, a supersonic washer was used to apply audio stimulus of at least 90 dB for one minute. The wild running (WR), clonic seizures (clonus), tonic seizures (tonus), and respiratory arrest (RA) were evaluated. The seizure suppressing action was evaluated from the rate or suppression of the average value of the seizure score found from 0 = no response, 1 = WR, 2 = clonus, 3 = tonus, and 4 = RA.

[0201] The results are shown in Table 4.

Table 4

Compound no.	Antiseizure action (suppression rate %) (compound 10 mg/kg, i.p.)
18	27.9
19	53.6
21	77.3
22	85.7
24	49.1
25	72
26	78
27	34

Table 4 (continued)

Compound no.	Antiseizure action (suppression rate %) (compound 10 mg/kg, i.p.)
28	56.9
29	66.2
31	48
32	94
34 (Ref.)	34
41	42.7
42 (Ref.)	60
46	27.9
47	64.1
48	53.6
49	60
50	72
51 (Ref.)	71.4
52 (Ref.)	20
55	62
56	50
58	66
62	44
63	76
64	94
65	72
66	39.2
67	37
69	64.7
70	73.9
71	32
73	52.2
74	44.4
75	99
77	85.7
78	66
79	79.8
80	66.3
81	61
82	71.9
Ref. = Reference compound	

Dopamine D_2 Receptor Blocking Action

[0202] 57 µl of the membrane fraction prepared from the striatum of Wister male rats (6 weeks old) was incubated in a buffer at 25°C for one hour along with the compound and 1.0 nM [^{3}H] raclopride. A GF/C glass filter (0.1% polyethylene imine treatment) was used for separation of the B and F, then the radioactivity was measured by a beta plate and the effect of the compound was evaluated.

[0203] The results are shown in Table 5.

Table 5

Compound no.	Dopamine D_2 receptor blocking action IC_{50} (nM)
21	2680
26	3370
32	3380
47	3960
49	987
Flunarizine	228

Acute Toxicity Test

[0204] Medicine was intravenously administered to ddY mice (male, 6 weeks old). The 50 percent lethal dosage LD_{50} of the acute toxicity was calculated by an ordinary method from the death rate up to 24 hours after administration.

[0205] The results are shown in Table 6.

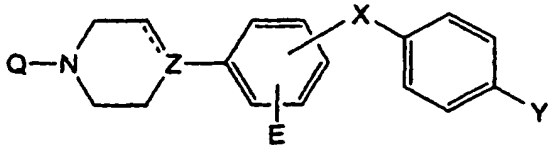
Table 6

Compound no.	LD_{50} (mg/kg, i.v.)
21	40.9
26	32.9
32	32.9
47	43.2

[0206] As explained above, the present invention can provide medicaments for the alleviation or treatment of symptoms based on ischemic diseases and symptoms derived from seizures, epilepsy, and migraine which have a powerful action in suppressing cytotoxic Ca^{2+} overload and which are free from side effects.

Claims

1. A medicament for the alleviation or treatment of symptoms based on ischemic diseases or symptoms derived from seizures, epilepsy and migraine containing, as an effective ingredient, a compound having the formula (I) or its pharmaceutically acceptable salt:



(I)

wherein Q represents a group having the formula:

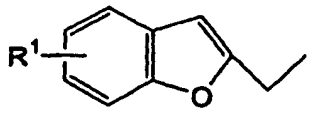
R-A-B-

in which R represents a hydrogen atom or a phehyl group, phenoxy group or benzoyl group each of which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

A represents a connecting bond, a C_3-C_6 cycloalkylene group, a C_2-C_4 alkenylene group which may be substituted by a C_1-C_3 alkyl group, a di(C_1-C_5 alkoxy)methylene group, or a hydroxyiminomethylene group, and

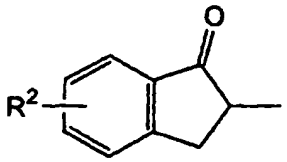
B represents a C_1-C_6 alkylene group which may be substituted by a hydroxyl group or a C_1-C_5 alkoxy group;

a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group; or

a group having the formula:



in which R^2 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group;

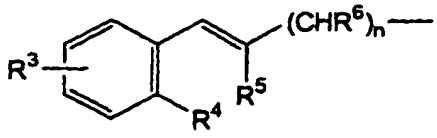
X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring being in a para position,

E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

the dotted line shows the presence or absence of a bond, when said dotted line shows the presence of a bond, Z represents a carbon atom, and when said dotted line shows the absence of a bond, Z represents CH or a nitrogen atom.

2. A medicament for the alleviation or treatment of symptoms based on ischemic diseases or symptoms derived from seizures, epilepsy and migraine as claimed in claim 1, wherein, in the formula (I),

Q represents a group having the formula:

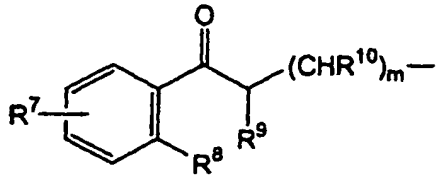


in which R^3 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group,

R^4 and R^5 are the same or different from each other and represent a hydrogen atom or a C_1-C_3 alkyl group,

or R^4 and R^5 are taken together to represent -O-,
R^6 represents a hydrogen atom, a hydroxyl group, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group, and
n is an integer of 1 to 6.

3. A medicament for the alleviation or treatment of symptoms based on ischemic diseases or symptoms derived from seizures, epilepsy and migraine as claimed in claim 1, wherein, in the formula (I), Q represents a group having the formula:



in which R^7 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group,
R^8 and R^9 are the same or different from each other and represent a hydrogen atom or a C_1-C_5 alkyl group, or R^8 and R^9 are taken together to represent a methylene group,
R^{10} represents a hydrogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group, and
m is an integer of 0 to 6.

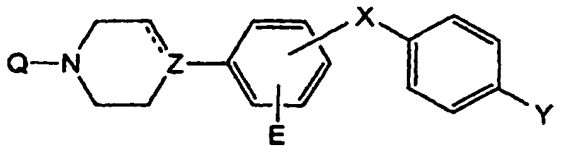
4. A medicament for the alleviation or treatment of symptoms based on ischemic diseases or symptoms derived from seizures, epilepsy and migraine as claimed in claim 1, wherein, in the formula (I), R represents a phenyl group which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom, and A represents a C_2-C_4 alkenylene group.

5. A medicament for the alleviation or treatment of symptoms based on ischemic diseases or symptoms derived from seizures, epilepsy and migraine as claimed in claim 1, wherein, in the formula (I), R represents a benzoyl group which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom, and A represents a connecting bond.

6. A medicament for the alleviation or treatment of symptoms based on ischemic diseases or symptoms derived from seizures, epilepsy and migraine as claimed in claim 1, wherein, in the formula (I), R represents a phenyl group which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom, A represents a connecting bond, and B represents a dimethylene group which is substituted by a hydroxyl group.

7. A medicament for the alleviation or treatment of symptoms based on ischemic diseases or symptoms derived from seizures, epilepsy and migraine as claimed in claim 1, wherein, in the formula (I), R represents a phenoxy group which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom, A represents a connecting bond, and B represents a trimethylene group which is substituted by a hydroxyl group.

8. Use for the manufacture of a medicament for the alleviation or treatment of symptoms based on ischemic diseases or symptoms derived from seizures, epilepsy and migraine of a compound having the formula (I) or its pharmaceutically acceptable salt:



(I)

wherein Q represents a group of the formula:

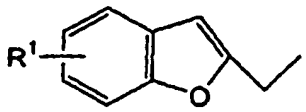
R-A-B-

in which R represents a hydrogen atom or a phenyl group, phenoxy group or benzoyl group each of which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

A represents a connecting bond, a C_3-C_6 cycloalkylene group, a C_2-C_4 alkenylene group which may be substituted by a C_1-C_3 alkyl group, a di(C_1-C_5 alkoxy)methylene group, or a hydroxyiminomethylene group, and

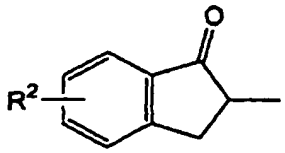
B represents a C_1-C_6 alkylene group which may be substituted by a hydroxyl group or a C_1-C_5 alkoxy group;

a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group; or

a group having the formula:



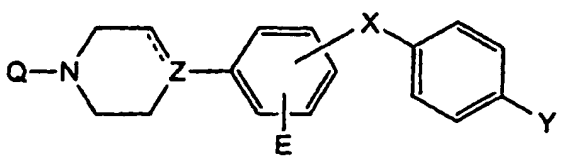
in which R^2 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group;

X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring being in a para position,

E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

the dotted line shows the presence or absence of a bond, when said dotted line shows the presence of a bond, Z represents a carbon atom, and when said dotted line shows the absence of a bond, Z represents CH or a nitrogen atom.

9. A Ca^{2+} overload suppressant containing, as an effective ingredient, a compound of the formula (I) or its pharmaceutically acceptable salt:



(I)

wherein Q represents a group having the formula:

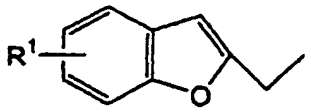
R-A-B-

in which R represents a hydrogen atom or a phenyl group, phenoxy group or benzoyl group each of which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

A represents a connecting bond, a C_3-C_6 cycloalkylene group, a C_2-C_4 alkenylene group which may be substituted by a C_1-C_3 alkyl group, a di(C_1-C_5 alkoxy)methylene group, or a hydroxyiminomethylene group, and

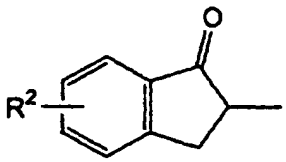
B represents a C_1-C_6 alkylene group which may be substituted by a hydroxyl group or a C_1-C_5 alkoxy group;

a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group; or

a group having the formula:



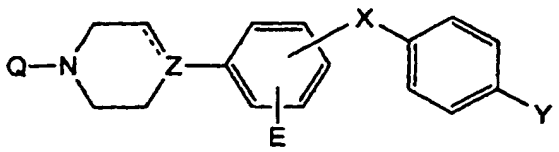
in which R^2 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group;

X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring being in a para position,

E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

the dotted line shows the presence or absence of a bond, when said dotted line shows the presence of a bond, Z represents a carbon atom, and when said dotted line shows the absence of a bond, Z represents CH or a nitrogen atom.

10. Use for the manufacture of a Ca^{2+} overload suppressant of a compound having the formula (I) or its pharmaceutically acceptable salt:



(I)

wherein Q represents a group having the formula:

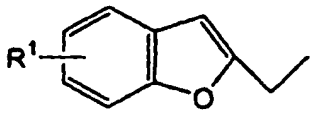
R-A-B-

in which R represents a hydrogen atom or a phenyl group, phenoxy group or benzoyl group each of which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

A represents a connecting bond, a C_3-C_6 cycloalkylene group, a C_2-C_4 alkenylene group which may be substituted by a C_1-C_3 alkyl group, a di(C_1-C_5 alkoxy)methylene group, or a hydroxyiminomethylene group, and

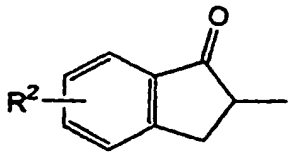
B represents a C_1-C_6 alkylene group which may be substituted by a hydroxyl group or a C_1-C_5 alkoxy group;

a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group; or

a group having the formula:



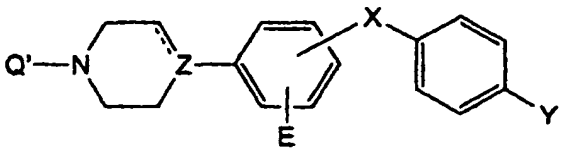
in which R^2 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group;

X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring being in a para position,

E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

the dotted line shows the presence or absence of a bond, when said dotted line shows the presence of a bond, Z represents a carbon atom, and when said dotted line shows the absence of a bond, Z represents CH or a nitrogen atom.

11. A compound having the formula (I') or its salts:



(I')

wherein Q' represents a group having the formula:

R'-A-B-

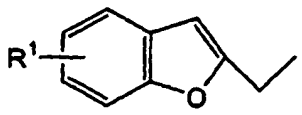
in which R' represents a phenyl group, phenoxy group or benzoyl group each of which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

A represents a connecting bond, a C_3-C_6 cycloalkylene group, a C_2-C_4 alkenylene group which may be

substituted by a C_1-C_3 alkyl group, a di(C_1-C_5 alkoxy)methylene group, or a hydroxyiminomethylene group, and

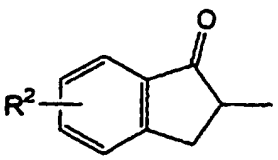
B represents a C_1-C_6 alkylene group which may be substituted by a hydroxyl group or a C_1-C_5 alkoxy group;

a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group; or

a group having the formula:



in which R^2 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group;

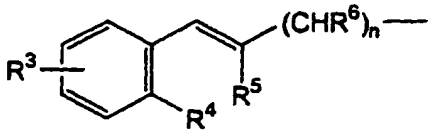
X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring being in a para position,

E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

the dotted line shows the presence or absence of a bond, when said dotted line shows the presence of a bond, Z represents a carbon atom, when said dotted line shows the absence of a bond, Z represents CH or a nitrogen atom,

when Z is a carbon atom or CH, X is a methylene group, A is a connecting bond, and B is an unsubstituted alkylene group, R' does not represent an unsubstituted phenyl group.

12. A compound or its salt as claimed in claim 11, wherein, in the formula (I'), Q' represents a group having the formula:



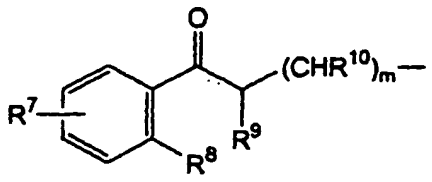
in which R^3 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group,

R^4 and R^5 are the same or different from each other and represent a hydrogen atom or a C_1-C_3 alkyl group, or R^4 and R^5 are taken together to represent -O-,

R^6 represents a hydrogen atom, a hydroxyl group, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group, and

n is an integer of 1 to 6.

13. A compound or its salt as claimed in claim 11, wherein, in the formula (I'), Q' represents a group having the formula:



in which R^7 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group,

R^8 and R^9 are the same or different from each other and represent a hydrogen atom or a C_1-C_5 alkyl group, or R^8 and R^9 are taken together to represent a methylene group,

R^{10} represents a hydrogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group, and

m is an integer of 0 to 6.

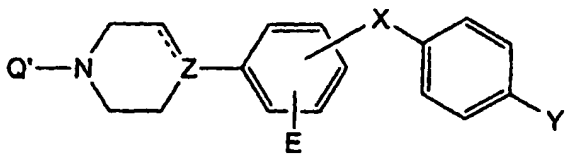
14. A compound or its salt as claimed in claim 11, wherein, in the formula (I'), R' represents a phenyl group which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom, and A represents a C_2-C_4 alkenylene group.

15. A compound or its salt as claimed in claim 11, wherein, in the formula (I'), R' represents a benzoyl group which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom, and A represents a connecting bond.

16. A compound or its salt as claimed in claim 11, wherein, in the formula (I'), R' represents a phenyl group which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom, A represents a connecting bond, and B represents a dimethylene group which is substituted by a hydroxyl group.

17. A compound or its salt as claimed in claim 11, wherein, in the formula (I'), R' represents a phenoxy group which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom, A represents a connecting bond, and B represents a trimethylene group which is substituted by a hydroxyl group.

18. A pharmaceutical composition containing, as an effective ingredient, a compound having the formula (I') or its pharmaceutically acceptable salt:



(I')

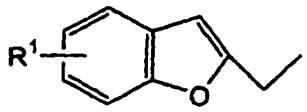
wherein Q' represents a group having the formula:

R'-A-B-

in which R' represents a phenyl group, phenoxy group or benzoyl group each of which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

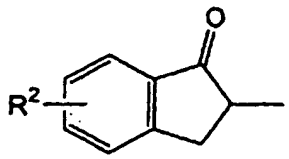
A represents a connecting bond, a C_3-C_6 cycloalkylene group, a C_2-C_4 alkenylene group which may be substituted by a C_1-C_3 alkyl group, a di(C_1-C_5 alkoxy)methylene group, or a hydroxyiminomethylene group, and

B represents a C_1-C_6 alkylene group which may be substituted by a hydroxyl group or a C_1-C_5 alkoxy group; a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group; or

a group having the formula:



in which R^2 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group;

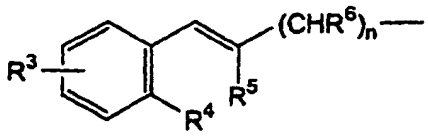
X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring being in a para position,

E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

the dotted line shows the presence or absence of a bond, when said dotted line shows the presence of a bond, Z represents a carbon atom, when said dotted line shows the absence of a bond, Z represents CH or a nitrogen atom,

when Z is a carbon atom or CH, X is a methylene group, A is a connecting bond, and B is an unsubstituted alkylene group, R' does not represent an unsubstituted phenyl group.

19. A pharmaceutical composition as claimed in claim 18, wherein, in the formula (I'), Q' represents a group having the formula:



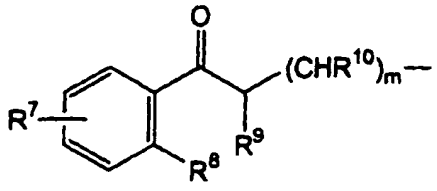
in which R^3 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group,

R^4 and R^5 are the same or different from each other and represent a hydrogen atom or a C_1-C_3 alkyl group, or R^4 and R^5 are taken together to represent -O-,

R^6 represents a hydrogen atom, a hydroxyl group, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group, and

n is an integer of 1 to 6.

20. A pharmaceutical composition as claimed in claim 18, wherein, in the formula (I'), Q' represents a group having the formula:



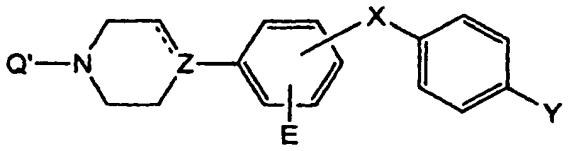
in which R^7 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group,

R^8 and R^9 are the same or different from each other and represent a hydrogen atom or a C_1-C_5 alkyl group, or R^8 and R^9 are taken together to represent a methylene group,

R^{10} represents a hydrogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group, and

m is an integer of 0 to 6.

21. A medicament for the alleviation or treatment of symptoms based on ischemic diseases or symptoms derived from seizures, epilepsy and migraine containing, as an effective ingredient, a compound having the formula (I') or its pharmaceutically acceptable salt:



(I')

wherein Q' represents a group having the formula:

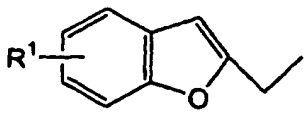
R'-A-B-

in which R' represents a phenyl group, phenoxy group or benzoyl group each of which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

A represents a connecting bond, a C_3-C_6 cycloalkylene group, a C_2-C_4 alkenylene group which may be substituted by a C_1-C_3 alkyl group, a di(C_1-C_5 alkoxy)methylene group, or a hydroxyiminomethylene group, and

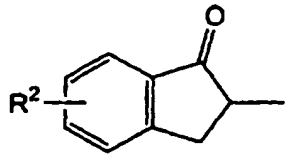
B represents a C_1-C_6 alkylene group which may be substituted by a hydroxyl group or a C_1-C_5 alkoxy group;

a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group; or

a group having the formula:



in which R^2 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group;

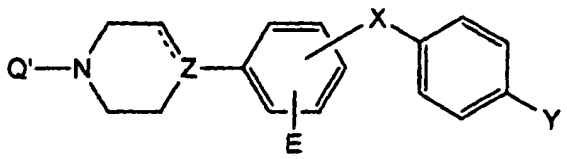
X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring being in a para position,

E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

the dotted line shows the presence or absence of a bond, when said dotted line shows the presence of a bond, Z represents a carbon atom, when said dotted line shows the absence of a bond, Z represents CH or a nitrogen atom,

when Z is a carbon atom or CH, X is a methylene group, A is a connecting bond, and B is an unsubstituted alkylene group, R' does not represent an unsubstituted phenyl group.

22. A Ca^{2+} overload suppressant containing, as its effective ingredient, a compound of the formula (I') or its pharmaceutically acceptable salt:



(I')

wherein, Q' represents a group having the formula:

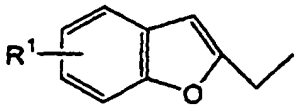
R'-A-B-

in which R' represents a phenyl group, phenoxy group or benzoyl group each of which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

A represents a connecting bond, a C_3-C_6 cycloalkylene group, a C_2-C_4 alkenylene group which may be substituted by a C_1-C_3 alkyl group, a di(C_1-C_5 alkoxy)methylene group, or a hydroxyiminomethylene group, and

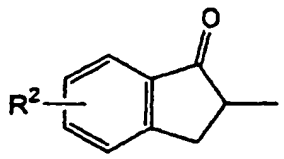
B represents a C_1-C_6 alkylene group which may be substituted by a hydroxyl group or a C_1-C_5 alkoxy group;

a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group; or

a group having the formula:



in which R^2 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group;

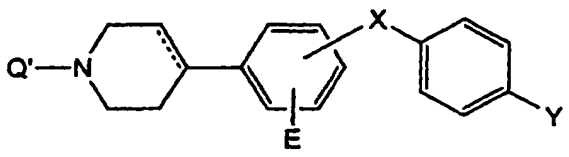
X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring being in a para position,

E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

the dotted line shows the presence or absence of a bond, when said dotted line shows the presence of a bond, Z represents a carbon atom, when said dotted line shows the absence of a bond, Z represents CH or a nitrogen atom,

when Z is a carbon atom or CH, X is a methylene group, A is a connecting bond, and B is an unsubstituted alkylene group, R' does not represent an unsubstituted phenyl group.

23. A compound having the formula (I") or its salts:



(I")

wherein Q' represents a group having the formula:

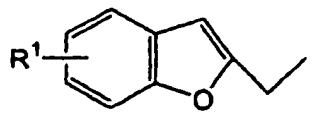
R'-A-B-

in which R' represents a phenyl group, phenoxy group or benzoyl group each of which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

A represents a connecting bond, a C_3-C_6 cycloalkylene group, a C_2-C_4 alkenylene group which may be substituted by a C_1-C_3 alkyl group, a di(C_1-C_5 alkoxy)methylene group, or a hydroxyiminomethylene group, and

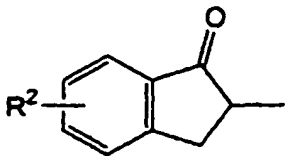
B represents a C_1-C_6 alkylene group which may be substituted by a hydroxyl group or a C_1-C_5 alkoxy group;

a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group; or

a group having the formula:



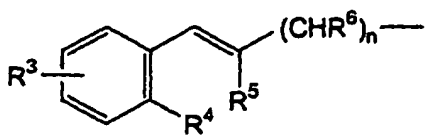
in which R^2 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group;

X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring being in a para position,

E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

the dotted line shows the presence or absence of a bond, and when X is a methylene group, A is a connecting bond and B is an unsubstituted alkylene group, R' does not represent an unsubstituted phenyl group.

24. A compound or its salt as claimed in claim 23, wherein, in the formula (I"), Q' represents a group having the formula:



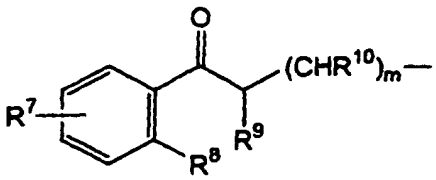
in which R^3 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group,

R^4 and R^5 are the same or different from each other and represent a hydrogen atom or a C_1-C_3 alkyl group, or R^4 and R^5 are taken together to represent -O-,

R^6 represents a hydrogen atom, a hydroxyl group, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group, and

n is an integer of 1 to 6.

25. A compound or its salt as claimed in claim 23, wherein, in the formula (I"), Q' represents a group having the formula:



in which R^7 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group,

R^8 and R^9 are the same or different from each other and represent a hydrogen atom or a C_1-C_5 alkyl group, or R^8 and R^9 are taken together to represent a methylene group,

R^{10} represents a hydrogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group, and

m is an integer of 0 to 6.

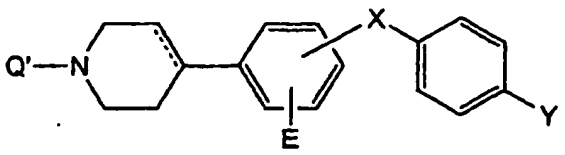
26. A compound or its salt as claimed in claim 23, wherein, in the formula (I"), R' represents a phenyl group which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom, and A represents a C_2-C_4 alkenylene group.

27. A compound or its salt as claimed in claim 23, wherein, in the formula (I"), R' represents a benzoyl group which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom, and A represents a connecting bond.

28. A compound or its salt as claimed in claim 23, wherein, in the formula (I"), R' represents a phenyl group which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom, A represents a connecting bond, and B represents a dimethylene group which is substituted by a hydroxyl group.

29. A compound or its salt as claimed in claim 23, wherein, in the formula (II"), R' represents a phenoxy group which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom, A represents a connecting bond, and B represents a trimethylene group which is substituted by a hydroxyl group.

30. A pharmaceutical composition containing, as an effective ingredient, a compound having the formula (I") or its pharmaceutically acceptable salt:



(I")

wherein Q' represents a group having the formula:

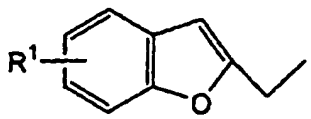
R'-A-B-

in which R' represents a phenyl group, phenoxy group or benzoyl group each of which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

A represents a connecting bond, a C_3-C_6 cycloalkylene group, a C_2-C_4 alkenylene group which may be substituted by a C_1-C_3 alkyl group, a di(C_1-C_5 alkoxy)methylene group, or a hydroxyiminomethylene group, and

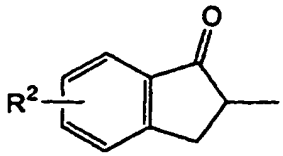
B represents a C_1-C_6 alkylene group which may be substituted by a hydroxyl group or a C_1-C_5 alkoxy group;

a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group; or

a group having the formula:



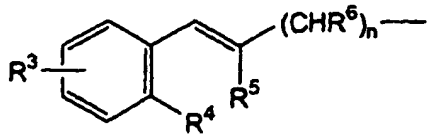
in which R^2 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group;

X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring being in a para position,

E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

the dotted line shows the presence or absence of a bond, and when X is a methylene group, A is a connecting bond and B is an unsubstituted alkylene group, R' does not represent an unsubstituted phenyl group.

31. A pharmaceutical composition as claimed in claim 30, wherein, in the formula (I"), Q' represents a group having the formula:



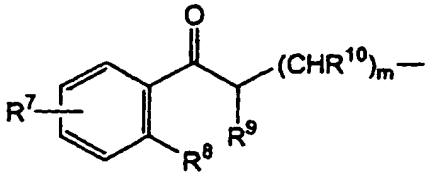
in which R^3 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group,

R^4 and R^5 are the same or different from each other and represent a hydrogen atom or a C_1-C_3 alkyl group, or R^4 and R^5 are taken together to represent -O-,

R^6 represents a hydrogen atom, a hydroxyl group, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group, and

n is an integer of 1 to 6.

32. A pharmaceutical composition as claimed in claim 30, wherein, in the formula (I"), Q' represents a group having the formula:



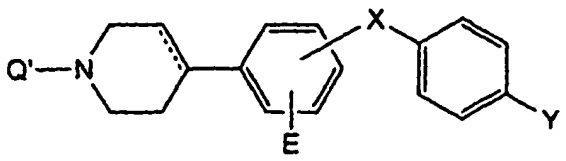
in which R^7 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group,

R^8 and R^9 are the same or different from each other and represent a hydrogen atom or a C_1-C_5 alkyl group, or R^8 and R^9 are taken together to represent a methylene group,

R^{10} represents a hydrogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group, and

m is an integer of 0 to 6.

33. A medicament for the alleviation or treatment of symptoms based on ischemic diseases or symptoms derived from seizures, epilepsy and migraine containing, as an effective ingredient, a compound having the formula (I") or its pharmaceutically acceptable salt:



(I")

wherein Q' represents a group having the formula:

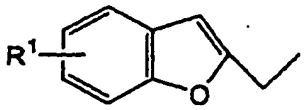
R'-A-B-

in which R' represents a phenyl group, phenoxy group or benzoyl group each of which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

A represents a connecting bond, a C_3-C_6 cycloalkylene group, a C_2-C_4 alkenylene group which may be substituted by a C_1-C_3 alkyl group, a di(C_1-C_5 alkoxy)methylene group, or a hydroxyiminomethylene group, and

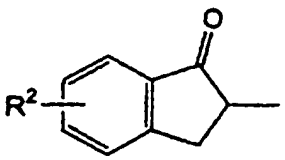
B represents a C_1-C_6 alkylene group which may be substituted by a hydroxyl group or a C_1-C_5 alkoxy group;

a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group; or

a group having the formula:



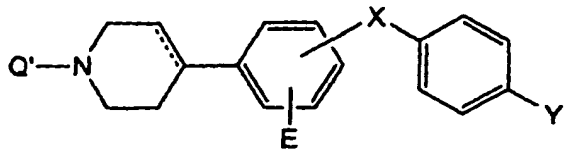
in which R^2 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group;

X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring being in a para position,

E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

the dotted line shows the presence or absence of a bond, and when X is a methylene group, A is a connecting bond and B is an unsubstituted alkylene group, R' does not represent an unsubstituted phenyl group.

34. A Ca^{2+} overload suppressant containing, as an effective ingredient, a compound having the general formula (I") or its pharmaceutically acceptable salt:



(I")

wherein Q' represents a group having the formula:

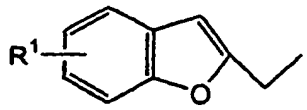
R'-A-B-

in which R' represents a phenyl group, phenoxy group or benzoyl group each of which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

A represents a connecting bond, a C_3-C_6 cycloalkylene group, a C_2-C_4 alkenylene group which may be substituted by a C_1-C_3 alkyl group, a di(C_1-C_5 alkoxy)methylene group, or a hydroxyiminomethylene group, and

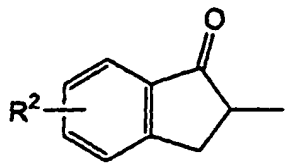
B represents a C_1-C_6 alkylene group which may be substituted by a hydroxyl group or a C_1-C_5 alkoxy group;

a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group; or

a group having the formula:



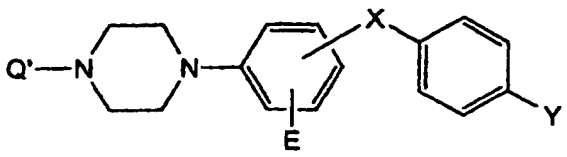
in which R^2 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group;

X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring being in a para position,

E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

the dotted line shows the presence or absence of a bond, and when X is a methylene group, A is a connecting bond and B is an unsubstituted alkylene group, R' does not represent an unsubstituted phenyl group.

35. A compound having the formula (I'") or its salt:



(I''')

wherein Q' represents a group having the formula:

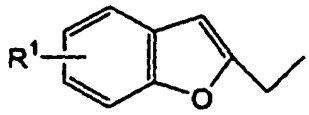
R'-A-B-

in which R' represents a phenyl group, phenoxy group or benzoyl group each of which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

A represents a connecting bond, a C_3-C_6 cycloalkylene group, a C_2-C_4 alkenylene group which may be substituted by a C_1-C_3 alkyl group, a di(C_1-C_5 alkoxy)methylene group, or a hydroxyiminomethylene group, and

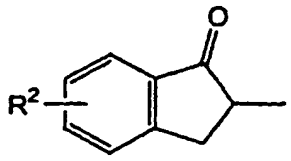
B represents a C_1-C_6 alkylene group which may be substituted by a hydroxyl group or a C_1-C_5 alkoxy group;

a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group; or

a group having the formula:

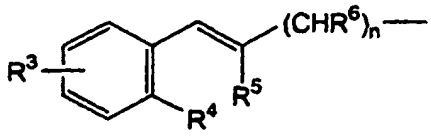


in which R^2 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group;

X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring being in a para position,

E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom.

36. A compound or its salt as claimed in claim 35, wherein, in the formula (I'''), Q' represents a group having the formula:



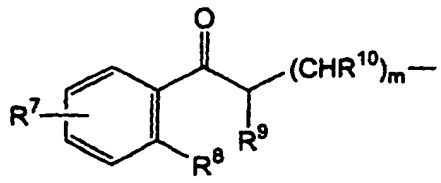
in which R^3 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group,

R^4 and R^5 are the same or different from each other and represent a hydrogen atom or a C_1-C_3 alkyl group, or R^4 and R^5 are taken together to represent -O-,

R^6 represents a hydrogen atom, a hydroxyl group, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group, and

n is an integer of 1 to 6.

37. A compound or its salt as claimed in claim 35, wherein, in the formula (I'''), Q' represents a group having the formula:



in which R^7 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group,

R^8 and R^9 are the same or different from each other and represent a hydrogen atom or a C_1-C_5 alkyl group, or R^8 and R^9 are taken together to represent a methylene group,

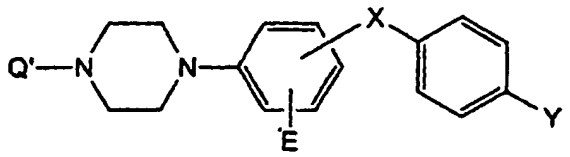
R^{10} represents a hydrogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group, and

m is an integer of 0 to 6.

38. A compound or its salt as claimed in claim 35, wherein, in the formula (I'''), R' represents a phenyl group which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom, and A represents a C_2-C_4 alkenylene group.

39. A compound or its salt as claimed in claim 35, wherein, in the formula (I'''), R' represents a benzoyl group which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom, and A represents a connecting bond.

40. A pharmaceutical composition containing, as an effective ingredient, a compound having the formula (I''') or its salt:



(I''')

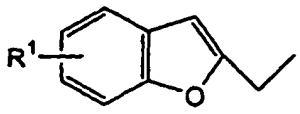
wherein, Q' represents a group having the formula:

R'-A-B-

in which R' represents a phenyl group, phenoxy group or benzoyl group each of which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom

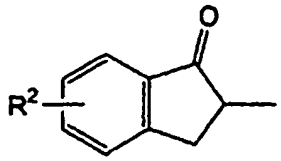
A represents a connecting bond, a C_3-C_6 cycloalkylene group, a C_2-C_4 alkenylene group which may be substituted by a C_1-C_3 alkyl group, a di(C_1-C_5 alkoxy)methylene group, or a hydroxyiminomethylene group, and

B represents a C_1-C_6 alkylene group which may be substituted by a hydroxyl group or a C_1-C_5 alkoxy group; a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group; or

a group having the formula:

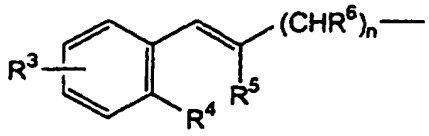


in which R^2 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group;

X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring being in a para position,

E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom.

41. A pharmaceutical composition as claimed in claim 40, wherein, in the formula (I'''), Q' represents a group having the formula:



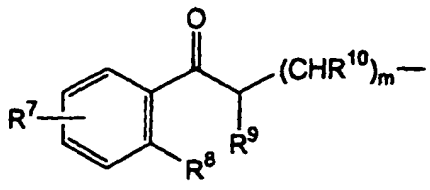
in which R^3 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group,

R^4 and R^5 are the same or different from each other and represent a hydrogen atom or a C_1-C_3 alkyl group, or R^4 and R^5 are taken together to represent -O-,

R^6 represents a hydrogen atom, a hydroxyl group, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group, and

n is an integer of 1 to 6.

42. A pharmaceutical composition as claimed in claim 40, wherein, in the formula (I'''), Q' represents a group having the formula:



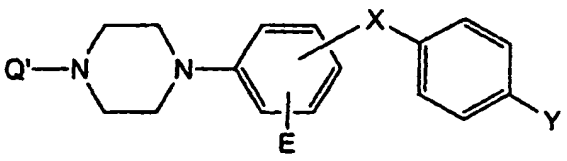
in which R^7 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group,

R^8 and R^9 are the same or different from each other and represent a hydrogen atom or a C_1-C_5 alkyl group, or R^8 and R^9 are taken together to represent a methylene group,

R^{10} represents a hydrogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group, and

m is an integer of 0 to 6.

43. A medicament for the alleviation or treatment of symptoms based on ischemic diseases or symptoms derived from seizures, epilepsy and migraine containing, as an effective ingredient, a compound having the general formula (I'") or its pharmaceutically acceptable salt:



(I'")

wherein, Q' represents a group having the formula:

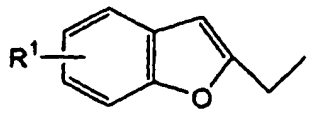
R'-A-B-

in which R' represents a phenyl group, phenoxy group or benzoyl group each of which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

A represents a connecting bond, a C_3-C_6 cycloalkylene group, a C_2-C_4 alkenylene group which may be substituted by a C_1-C_3 alkyl group, a di(C_1-C_5 alkoxy)methylene group, or a hydroxyiminomethylene group, and

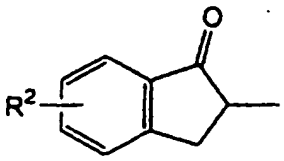
B represents a C_1-C_6 alkylene group which may be substituted by a hydroxyl group or a C_1-C_5 alkoxy group;

a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group; or

a group having the formula:

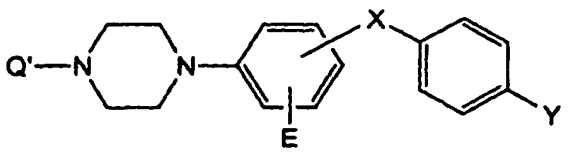


in which R^2 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group;

X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring being in a para position,

E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom.

44. A Ca^{2+} overload suppressant containing, as an effective ingredient, a compound having the formula (I'") or its pharmaceutically acceptable salt:



(I'")

wherein Q' represents a group having the formula:

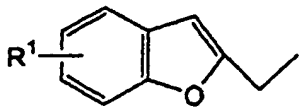
R'-A-B-

in which R' represents a phenyl group, phenoxy group or benzoyl group each of which may be substituted by a halogen atom, a hydroxyl group, a C_1-C_5 alkoxy group or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

A represents a connecting bond, a C_3-C_6 cycloalkylene group, a C_2-C_4 alkenylene group which may be substituted by a C_1-C_3 alkyl group, a di(C_1-C_5 alkoxy)methylene group, or a hydroxyiminomethylene group, and

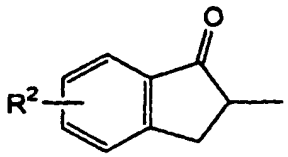
B represents a C_1-C_6 alkylene group which may be substituted by a hydroxyl group or a C_1-C_5 alkoxy group;

a group having the formula:



in which R^1 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group; or

a group having the formula:

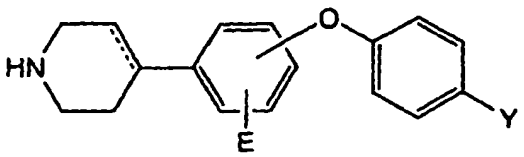


in which R^2 represents a hydrogen atom, a halogen atom, a C_1-C_5 alkyl group which may be substituted by a halogen atom, a C_1-C_5 alkoxy group, or a hydroxyl group;

X represents an oxygen atom or a methylene group, the substitution of X for the benzene ring being in a para position,

E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom.

45. A compound having the general formula (IIa) or its salt:



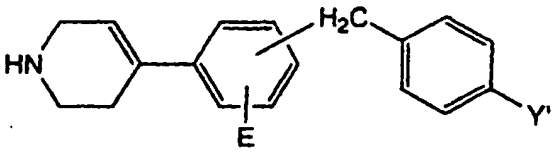
(IIa)

wherein E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

the dotted line shows the presence or absence of a bond,

and the substitution of the benzene ring bonding with the piperidine ring or the tetrahydropyridine ring and the group $-OC_6H_4Y$ is in a para position.

46. A compound having the formula (IIb) or its salt:

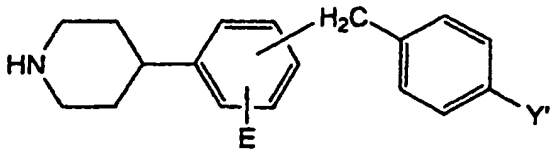


(IIb)

wherein E represents a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom, Y' represents a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

and the substitution of the benzene ring bonding with the tetrahydropyridine ring and the group $-CH_2C_6H_4Y'$ is in a para position.

47. A compound having the formula (IIc) or its salt:

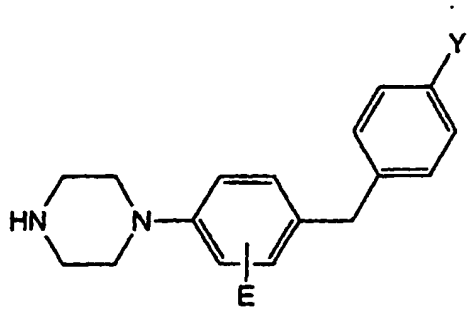


(IIc)

wherein E represents a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom, Y' represents a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom,

and the substitution of the benzene ring bonding with the piperidine ring and the group $-CH_2C_6H_4Y'$ is in a para position.

48. A compound having the formula (IIIa) or its salt:

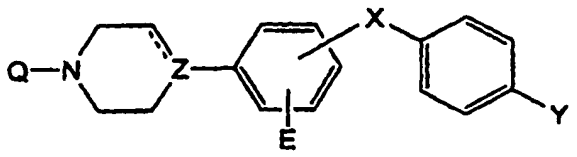


(IIIa)

wherein, E and Y may be the same or different from each other and represent a hydrogen atom, a hydroxyl group, a halogen atom, a C_1-C_5 alkoxy group, or a C_1-C_5 alkyl group which may be substituted by a halogen atom.

Patentansprüche

1. Medikament zur Linderung oder Behandlung von Symptomen auf Basis von ischämischen Krankheiten oder Symptomen, die aus Anfällen, Epilepsie und Migräne stammen, das als wirksamen Bestandteil eine Verbindung mit der Formel (I) oder ihr pharmazeutisch akzeptables Salz enthält:



(I)

worin Q eine Gruppe mit der Formel:

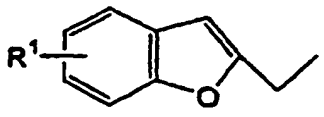
R-A-B-

worin R ein Wasserstoffatom oder eine Phenylgruppe, Phenoxygruppe oder Benzoylgruppe darstellt, von denen jede mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann,

A eine verbindende Bindung, eine C_{3-6}-Cycloalkylengruppe, eine C_{2-4}-Alkenylengruppe, die mit einer C_{1-3}-Alkylgruppe substituiert sein kann, eine Di-(C_{1-5}alkoxy)methylengruppe oder eine Hydroxyiminomethylengruppe darstellt und

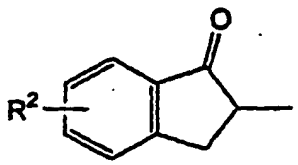
B eine C_{1-6}-Alkylengruppe darstellt, die mit einer Hydroxylgruppe oder einer C_{1-5}-Alkoxygruppe substituiert sein kann;

eine Gruppe mit der Formel:



worin R^1 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt; oder

eine Gruppe mit der Formel:



darstellt, worin R^2 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt;

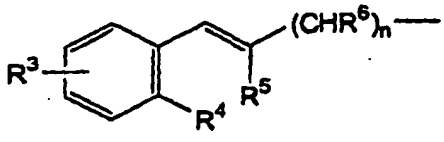
X ein Sauerstoffatom oder eine Methylengruppe darstellt, wobei die Substitution von X für den Benzolring in einer para-Position ist,

E und Y gleich oder verschieden sein können und ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellen,

die gestrichelte Linie die Gegenwart oder Abwesenheit einer Bindung zeigt, Z ein Kohlenstoffatom darstellt, wenn die gestrichelte Linie die Gegenwart einer Bindung zeigt, und Z CH oder ein Stickstoffatom darstellt, wenn die gestrichelte Linie die Abwesenheit einer Bindung zeigt.

2. Medikament zur Linderung oder Behandlung von Symptomen auf Basis von ischämischen Krankheiten oder Symptomen, die aus Anfällen, Epilepsie und Migräne stammen, gemäß Anspruch 1, worin in Formel (I)

Q eine Gruppe mit der Formel:



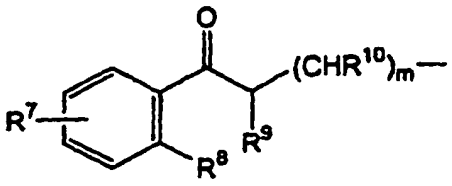
darstellt, worin R^3 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt,

R_4 und R_5 gleich oder verschieden sind und ein Wasserstoffatom oder eine C_{1-3}-Alkylgruppe darstellen oder R^4 und R^5 zusammen -O- darstellen,

R^6 ein Wasserstoffatom, eine Hydroxylgruppe, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe darstellt und

n eine ganze Zahl von 1 bis 6 ist.

3. Medikament zur Linderung oder Behandlung von Symptomen auf Basis von ischämischen Krankheiten oder Symptomen, die aus Anfällen, Epilepsie und Migräne stammen, gemäß Anspruch 1, worin in Formel (I) Q eine Gruppe mit der Formel:



darstellt, worin R^7 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt,

R^8 und R^9 gleich oder verschieden sind und ein Wasserstoffatom oder eine C_{1-5}-Alkylgruppe darstellen oder R^8 und R^9 zusammen eine Methylengruppe darstellen,

R^{10} ein Wasserstoffatom, eine Hydroxylgruppe, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe darstellt und

m eine ganze Zahl von 0 bis 6 ist.

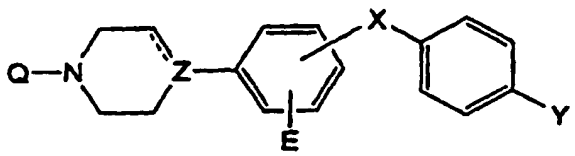
4. Medikament zur Linderung oder Behandlung von Symptomen auf Basis von ischämischen Krankheiten oder Symptomen, die aus Anfällen, Epilepsie und Migräne stammen, gemäß Anspruch 1, worin in Formel (I) R eine Phenylgruppe darstellt, die mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann, und A eine C_{2-4}-Alkenylengruppe darstellt.

5. Medikament zur Linderung oder Behandlung von Symptomen auf Basis von ischämischen Krankheiten oder Symptomen, die aus Anfällen, Epilepsie und Migräne stammen, gemäß Anspruch 1, worin in Formel (I) R eine Benzoylgruppe darstellt, die mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann, und A eine verbindende Bindung darstellt.

6. Medikament zur Linderung oder Behandlung von Symptomen auf Basis von ischämischen Krankheiten oder Symptomen, die aus Anfällen, Epilepsie und Migräne stammen, gemäß Anspruch 1, worin in Formel (I) R eine Phenylgruppe darstellt, die mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann, A eine verbindende Bindung darstellt und B eine Dimethylengruppe darstellt, die mit einer Hydroxylgruppe substituiert ist.

7. Medikament zur Linderung oder Behandlung von Symptomen auf Basis von ischämischen Krankheiten oder Symptomen, die aus Anfällen, Epilepsie und Migräne stammen, gemäß Anspruch 1, worin in Formel (I) R eine Phenoxygruppe darstellt, die mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann, A eine verbindende Bindung darstellt und B eine Trimethylengruppe darstellt, die mit einer Hydroxylgruppe substituiert ist.

8. Verwendung, zur Herstellung eines Medikaments zur Linderung oder Behandlung von Symptomen auf Basis von ischämischen Krankheiten oder Symptomen, die aus Anfällen, Epilepsie und Migräne stammen, einer Verbindung mit der Formel (I) oder ihres pharmazeutisch akzeptablen Salzes:



(I)

worin Q eine Gruppe mit der Formel:

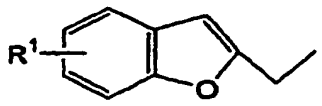
R-A-B-

worin R ein Wasserstoffatom oder eine Phenylgruppe, Phenoxygruppe oder Benzoylgruppe darstellt, von denen jede mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann,

A eine verbindende Bindung, eine C_{3-6}-Cycloalkylengruppe, eine C_{2-4}-Alkenylengruppe, die mit einer C_{1-3}-Alkylgruppe substituiert sein kann, eine Di-(C_{1-5}alkoxy)methylengruppe oder eine Hydroxyiminomethylengruppe darstellt und

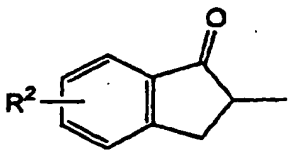
B eine C_{1-6}-Alkylengruppe darstellt, die mit einer Hydroxylgruppe oder einer C_{1-5}-Alkoxygruppe substituiert sein kann;

eine Gruppe mit der Formel:



worin R^1 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt; oder

eine Gruppe mit der Formel:



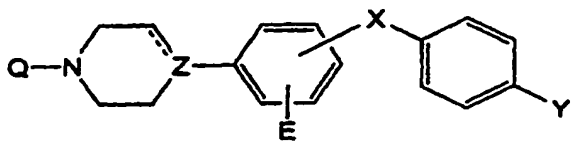
darstellt, worin R^2 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt;

X ein Sauerstoffatom oder eine Methylengruppe darstellt, wobei die Substitution von X für den Benzolring in einer para-Position ist,

E und Y gleich oder verschieden sein können und ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellen,

die gestrichelte Linie die Gegenwart oder Abwesenheit einer Bindung zeigt, Z ein Kohlenstoffatom darstellt, wenn die gestrichelte Linie die Gegenwart einer Bindung zeigt, und Z CH oder ein Stickstoffatom darstellt, wenn die gestrichelte Linie die Abwesenheit einer Bindung zeigt.

9. Ca^{2+}-Überladungssuppressivum, das als wirksamen Bestandteil eine Verbindung der Formel (I) oder ihr pharmazeutisch akzeptables Salz enthält:



(I)

worin Q eine Gruppe mit der Formel:

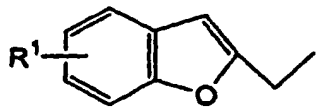
R-A-B-

worin R ein Wasserstoffatom oder eine Phenylgruppe, Phenoxygruppe oder Benzoylgruppe darstellt, von denen jede mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann,

A eine verbindende Bindung, eine C_{3-6}-Cycloalkylengruppe, eine C_{2-4}-Alkenylengruppe, die mit einer C_{1-3}-Alkylgruppe substituiert sein kann, eine Di-(C_{1-5}alkoxy)methylengruppe oder eine Hydroxyiminomethylengruppe darstellt und

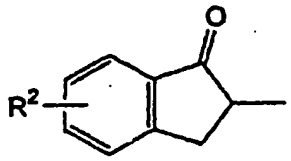
B eine C_{1-6}-Alkylengruppe darstellt, die mit einer Hydroxylgruppe oder einer C_{1-5}-Alkoxygruppe substituiert sein kann;

eine Gruppe mit der Formel:



worin R^1 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt; oder

eine Gruppe mit der Formel:



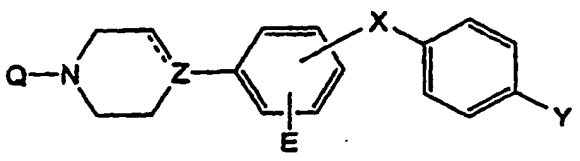
darstellt, worin R^2 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt;

X ein Sauerstoffatom oder eine Methylengruppe darstellt, wobei die Substitution von X für den Benzolring in einer para-Position ist,

E und Y gleich oder verschieden sein können und ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellen,

die gestrichelte Linie die Gegenwart oder Abwesenheit einer Bindung zeigt, Z ein Kohlenstoffatom darstellt, wenn die gestrichelte Linie die Gegenwart einer Bindung zeigt, und Z CH oder ein Stickstoffatom darstellt, wenn die gestrichelte Linie die Abwesenheit einer Bindung zeigt.

10. Verwendung, zur Herstellung eines Ca^{2+}-Überladungssuppressivums, einer Verbindung mit Formel (I) oder ihres pharmazeutisch akzeptablen Salzes:



(I)

worin Q eine Gruppe mit der Formel:

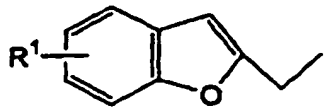
R-A-B-

worin R ein Wasserstoffatom oder eine Phenylgruppe, Phenoxygruppe oder Benzoylgruppe darstellt, von denen jede mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann,

A eine verbindende Bindung, eine C_{3-6}-Cycloalkylengruppe, eine C_{2-4}-Alkenylengruppe, die mit einer C_{1-3}-Alkylgruppe substituiert sein kann, eine Di-(C_{1-5}alkoxy)methylengruppe oder eine Hydroxyiminomethylengruppe darstellt und

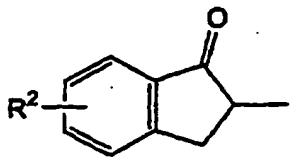
B eine C_{1-6}-Alkylengruppe darstellt, die mit einer Hydroxylgruppe oder einer C_{1-5}-Alkoxygruppe substituiert sein kann;

eine Gruppe mit der Formel:



worin R^1 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt; oder

eine Gruppe mit der Formel:



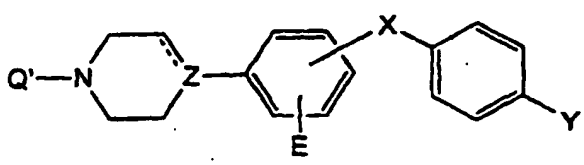
darstellt, worin R^2 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt;

X ein Sauerstoffatom oder eine Methylengruppe darstellt, wobei die Substitution von X für den Benzolring in einer para-Position ist,

E und Y gleich oder verschieden sein können und ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellen,

die gestrichelte Linie die Gegenwart oder Abwesenheit einer Bindung zeigt, Z ein Kohlenstoffatom darstellt, wenn die gestrichelte Linie die Gegenwart einer Bindung zeigt, und Z CH oder ein Stickstoffatom darstellt, wenn die gestrichelte Linie die Abwesenheit einer Bindung zeigt.

11. Verbindung mit der Formel (I') oder ihre Salze:



(I')

worin Q' eine Gruppe mit der Formel:

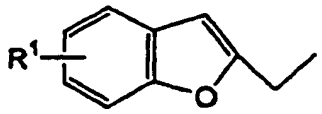
R'-A-B-

worin R' eine Phenylgruppe, Phenoxygruppe oder Benzoylgruppe darstellt, von denen jede mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann,

A eine verbindende Bindung, eine C_{3-6}-Cycloalkylengruppe, eine C_{2-4}-Alkenylengruppe, die mit einer C_{1-3}-Alkylgruppe substituiert sein kann, eine Di-(C_{1-5}alkoxy)methylengruppe oder eine Hydroxyiminomethylengruppe darstellt und

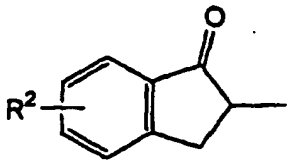
B eine C_{1-6}-Alkylengruppe darstellt, die mit einer Hydroxylgruppe oder einer C_{1-5}-Alkoxygruppe substituiert sein kann;

eine Gruppe mit der Formel:



worin R^1 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt; oder

eine Gruppe mit der Formel:



darstellt, worin R^2 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt;

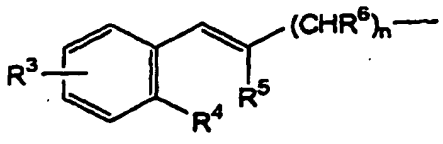
X ein Sauerstoffatom oder eine Methylengruppe darstellt, wobei die Substitution von X für den Benzolring in einer para-Position ist,

E und Y gleich oder verschieden sein können und ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellen,

die gestrichelte Linie die Gegenwart oder Abwesenheit einer Bindung zeigt, Z ein Kohlenstoffatom darstellt, wenn die gestrichelte Linie die Gegenwart einer Bindung zeigt, und Z CH oder ein Stickstoffatom darstellt, wenn die gestrichelte Linie die Abwesenheit einer Bindung zeigt,

wenn Z ein Kohlenstoffatom oder CH ist, X eine Methylengruppe ist, A eine verbindende Bindung ist und B eine unsubstituierte Alkylengruppe ist, R' keine unsubstituierte Phenylgruppe darstellt.

12. Verbindung oder ihr Salz gemäß Anspruch 11, worin in Formel (I') Q' eine Gruppe mit der Formel:



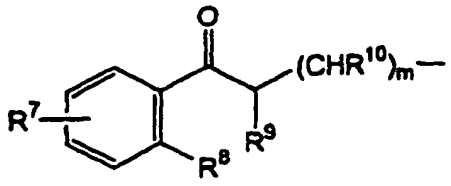
darstellt, worin R^3 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt,

R_4 und R_5 gleich oder verschieden sind und ein Wasserstoffatom oder eine C_{1-3}-Alkylgruppe darstellen oder R^4 und R^5 zusammen -O- darstellen,

R^6 ein Wasserstoffatom, eine Hydroxylgruppe, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe darstellt und

n eine ganze Zahl von 1 bis 6 ist.

13. Verbindung oder ihr Salz gemäß Anspruch 11, worin in Formel (I') Q' eine Gruppe mit der Formel



darstellt, worin R^7 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt,

R^8 und R^9 gleich oder verschieden sind und ein Wasserstoffatom oder eine C_{1-5}-Alkylgruppe darstellen oder R^8 und R^9 zusammen eine Methylengruppe darstellen,

R^{10} ein Wasserstoffatom, eine Hydroxylgruppe, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe darstellt und

m eine ganze Zahl von 0 bis 6 ist.

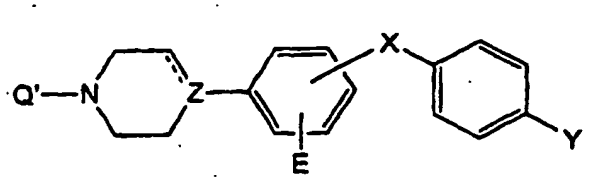
14. Verbindung oder ihr Salz gemäß Anspruch 11, worin in Formel (I') R' eine Phenylgruppe darstellt, die mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann, und A eine C_{2-4}-Alkenylengruppe darstellt.

15. Verbindung oder ihr Salz gemäß Anspruch 11, worin in Formel (I') R' eine Benzoylgruppe darstellt, die mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann, und A eine verbindende Bindung darstellt.

16. Verbindung oder ihr Salz gemäß Anspruch 11, worin in Formel (I') R' eine Phenylgruppe darstellt, die mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann, A eine verbindende Bindung darstellt und B eine Dimethylengruppe darstellt, die mit einer Hydroxylgruppe substituiert ist.

17. Verbindung oder ihr Salz gemäß Anspruch 11, worin in Formel (I') R' eine Phenoxygruppe darstellt, die mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann, A eine verbindende Bindung darstellt und B eine Trimethylengruppe darstellt, die mit einer Hydroxylgruppe substituiert ist.

18. Pharmazeutische Zusammensetzung, die als wirksamen Bestandteil eine Verbindung mit der Formel (I') oder ihr pharmazeutisch akzeptables Salz enthält:



(I')

worin Q' eine Gruppe mit der Formel:

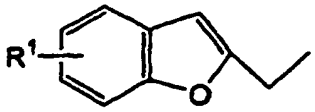
R'-A-B-

worin R' eine Phenylgruppe, Phenoxygruppe oder Benzoylgruppe darstellt, von denen jede mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann,

A eine verbindende Bindung, eine C_{3-6}-Cycloalkylengruppe, eine C_{2-4}-Alkenylengruppe, die mit einer C_{1-3}-Alkylgruppe substituiert sein kann, eine Di-(C_{1-5}alkoxy)methylengruppe oder eine Hydroxyiminomethylengruppe darstellt und

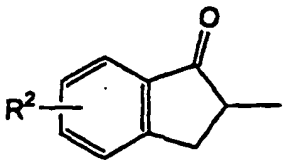
B eine C_{1-6}-Alkylengruppe darstellt, die mit einer Hydroxylgruppe oder einer C_{1-5}-Alkoxygruppe substituiert sein kann;

eine Gruppe mit der Formel:



worin R^1 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt; oder

eine Gruppe mit der Formel:



darstellt, worin R^2 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt;

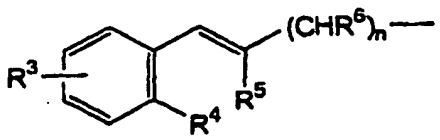
X ein Sauerstoffatom oder eine Methylengruppe darstellt, wobei die Substitution von X für den Benzolring in einer para-Position ist,

E und Y gleich oder verschieden sein können und ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellen,

die gestrichelte Linie die Gegenwart oder Abwesenheit einer Bindung zeigt, Z ein Kohlenstoffatom darstellt, wenn die gestrichelte Linie die Gegenwart einer Bindung zeigt, und Z CH oder ein Stickstoffatom darstellt, wenn die gestrichelte Linie die Abwesenheit einer Bindung zeigt,

wenn Z ein Kohlenstoffatom oder CH ist, X eine Methylengruppe ist, A eine verbindende Bindung ist und B eine unsubstituierte Alkylengruppe ist, R' keine unsubstituierte Phenylgruppe darstellt.

19. Pharmazeutische Zusammensetzung gemäß Anspruch 18, worin in Formel (I') Q' eine Gruppe mit der Formel:



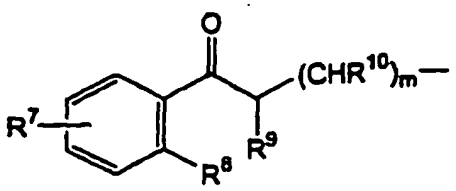
darstellt, worin R^3 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt,

R_4 und R_5 gleich oder verschieden sind und ein Wasserstoffatom oder eine C_{1-3}-Alkylgruppe darstellen oder R^4 und R^5 zusammen -O- darstellen,

R^6 ein Wasserstoffatom, eine Hydroxylgruppe, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe darstellt und

n eine ganze Zahl von 1 bis 6 ist.

20. Pharmazeutische Zusammensetzung gemäß Anspruch 18, worin in Formel (I') Q' eine Gruppe mit der Formel:



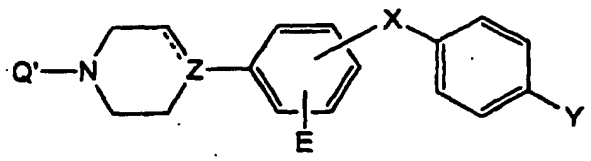
darstellt, worin R^7 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt,

R^8 und R^9 gleich oder verschieden sind und ein Wasserstoffatom oder eine C_{1-5}-Alkylgruppe darstellen oder R^8 und R^9 zusammen eine Methylengruppe darstellen,

R^{10} ein Wasserstoffatom, eine Hydroxylgruppe, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe darstellt und

m eine ganze Zahl von 0 bis 6 ist.

21. Medikament zur Linderung oder Behandlung von Symptomen auf Basis von ischämischen Krankheiten oder Symptomen, die aus Anfällen, Epilepsie und Migräne stammen, das als wirksamen Bestandteil eine Verbindung mit der Formel (I') oder ihr pharmazeutisch akzeptables Salz enthält:



(I')

worin Q' eine Gruppe mit der Formel:

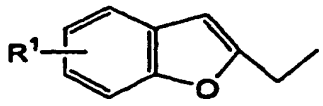
R'-A-B-

worin R' eine Phenylgruppe, Phenoxygruppe oder Benzoylgruppe darstellt, von denen jede mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann,

A eine verbindende Bindung, eine C_{3-6}-Cycloalkylengruppe, eine C_{2-4}-Alkenylengruppe, die mit einer C_{1-3}-Alkylgruppe substituiert sein kann, eine Di-(C_{1-5}alkoxy)methylengruppe oder eine Hydroxyiminomethylengruppe darstellt und

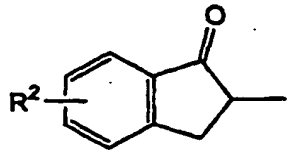
B eine C_{1-6}-Alkylengruppe darstellt, die mit einer Hydroxylgruppe oder einer C_{1-5}-Alkoxygruppe substituiert sein kann;

eine Gruppe mit der Formel:



worin R^1 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt; oder

eine Gruppe mit der Formel:



darstellt, worin R^2 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt;

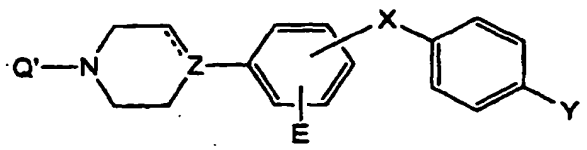
X ein Sauerstoffatom oder eine Methylengruppe darstellt, wobei die Substitution von X für den Benzolring in einer para-Position ist,

E und Y gleich oder verschieden sein können und ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellen,

die gestrichelte Linie die Gegenwart oder Abwesenheit einer Bindung zeigt, Z ein Kohlenstoffatom darstellt, wenn die gestrichelte Linie die Gegenwart einer Bindung zeigt, und Z CH oder ein Stickstoffatom darstellt, wenn die gestrichelte Linie die Abwesenheit einer Bindung zeigt,

wenn Z ein Kohlenstoffatom oder CH ist, X eine Methylengruppe ist, A eine verbindende Bindung ist und B eine unsubstituierte Alkylengruppe ist, R' keine unsubstituierte Phenylgruppe darstellt.

22. Ca^{2+}-Überladungssuppressivum, das als wirksamen Bestandteil eine Verbindung der Formel (I') oder ihr pharmazeutisch akzeptables Salz enthält:



(I')

worin Q' eine Gruppe mit der Formel:

R'-A-B-

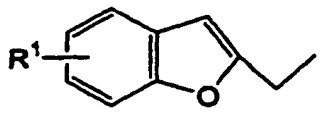
worin R' eine Phenylgruppe, Phenoxygruppe oder Benzoylgruppe darstellt, von denen jede mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann,

A eine verbindende Bindung, eine C_{3-6}-Cycloalkylengruppe, eine C_{2-4}-Alkenylengruppe, die mit einer C_{1-3}-Alkylgruppe substituiert sein kann, eine Di-(C_{1-5}alkoxy)methylengruppe oder eine Hydroxyiminomethylengruppe darstellt und

B eine C_{1-6}-Alkylengruppe darstellt, die mit einer Hydroxylgruppe oder einer C_{1-5}-Alkoxygruppe substituiert

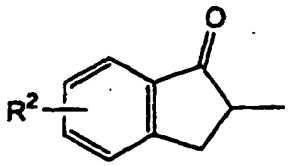
sein kann;

eine Gruppe mit der Formel:



worin R^1 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt; oder

eine Gruppe mit der Formel:



darstellt, worin R^2 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt;

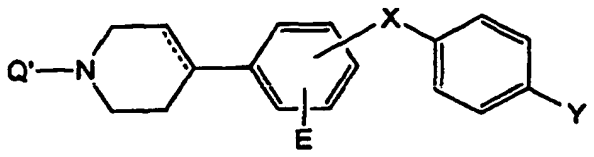
X ein Sauerstoffatom oder eine Methylengruppe darstellt, wobei die Substitution von X für den Benzolring in einer para-Position ist,

E und Y gleich oder verschieden sein können und ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellen,

die gestrichelte Linie die Gegenwart oder Abwesenheit einer Bindung zeigt, Z ein Kohlenstoffatom darstellt, wenn die gestrichelte Linie die Gegenwart einer Bindung zeigt, und Z CH oder ein Stickstoffatom darstellt, wenn die gestrichelte Linie die Abwesenheit einer Bindung zeigt,

wenn Z ein Kohlenstoffatom oder CH ist, X eine Methylengruppe ist, A eine verbindende Bindung ist und B eine unsubstituierte Alkylengruppe ist, R' keine unsubstituierte Phenylgruppe darstellt.

23. Verbindung mit der Formel (I") oder ihre Salze:



(I")

worin Q' eine Gruppe mit der Formel:

R'-A-B-

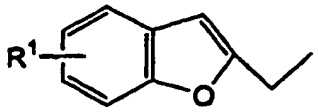
worin R' eine Phenylgruppe, Phenoxygruppe oder Benzoylgruppe darstellt, von denen jede mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann,

A eine verbindende Bindung, eine C_{3-6}-Cycloalkylengruppe, eine C_{2-4}-Alkenylengruppe, die mit einer C_{1-3}-Alkylgruppe substituiert sein kann, eine Di-(C_{1-5}alkoxy)methylengruppe oder eine Hydroxyiminomethylengruppe

darstellt und

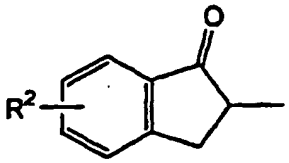
B eine C_{1-6}-Alkylengruppe darstellt, die mit einer Hydroxylgruppe oder einer C_{1-5}-Alkoxygruppe substituiert sein kann;

eine Gruppe mit der Formel:



worin R^1 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt; oder

eine Gruppe mit der Formel:



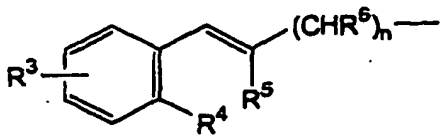
darstellt, worin R^2 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt;

X ein Sauerstoffatom oder eine Methylengruppe darstellt, wobei die Substitution von X für den Benzolring in einer para-Position ist,

E und Y gleich oder verschieden sein können und ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellen,

die gestrichelte Linie die Gegenwart oder Abwesenheit einer Bindung zeigt und R' keine unsubstituierte Phenylgruppe darstellt, wenn X eine Methylengruppe ist, A eine verbindende Bindung ist und B eine unsubstituierte Alkylengruppe ist.

24. Verbindung oder ihr Salz gemäß Anspruch 23, worin in Formel (I") Q' eine Gruppe mit der Formel:



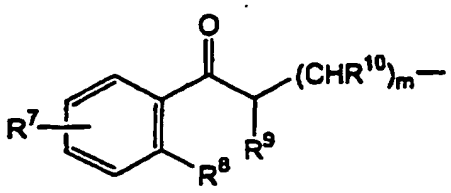
darstellt, worin R^3 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt,

R_4 und R_5 gleich oder verschieden sind und ein Wasserstoffatom oder eine C_{1-3}-Alkylgruppe darstellen oder R^4 und R^5 zusammen -O- darstellen,

R^6 ein Wasserstoffatom, eine Hydroxylgruppe, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe darstellt und

n eine ganze Zahl von 1 bis 6 ist.

25. Verbindung oder ihr Salz gemäß Anspruch 23, worin in Formel (I") Q' eine Gruppe mit der Formel



darstellt, worin R^7 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt,

R^8 und R^9 gleich oder verschieden sind und ein Wasserstoffatom oder eine C_{1-5}-Alkylgruppe darstellen oder R^8 und R^9 zusammen eine Methylengruppe darstellen,

R^{10} ein Wasserstoffatom, eine Hydroxylgruppe, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe darstellt und

m eine ganze Zahl von 0 bis 6 ist.

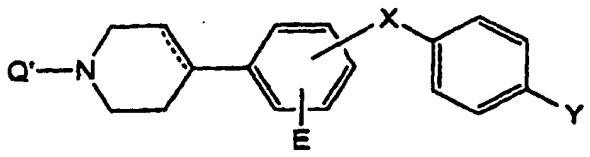
26. Verbindung oder ihr Salz gemäß Anspruch 23, worin in Formel (I") R' eine Phenylgruppe darstellt, die mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann, und A eine C_{2-4}-Alkenylengruppe darstellt.

27. Verbindung oder ihr Salz gemäß Anspruch 23, worin in Formel (I") R' eine Benzoylgruppe darstellt, die mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann, und A eine verbindende Bindung darstellt.

28. Verbindung oder ihr Salz gemäß Anspruch 23, worin in Formel (I") R' eine Phenylgruppe darstellt, die mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann, A eine verbindende Bindung darstellt und B eine Dimethylengruppe darstellt, die mit einer Hydroxylgruppe substituiert ist.

29. Verbindung oder ihr Salz gemäß Anspruch 23, worin in Formel (I") R' eine Phenoxygruppe darstellt, die mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann, A eine verbindende Bindung darstellt und B eine Trimethylengruppe darstellt, die mit einer Hydroxylgruppe substituiert ist.

30. Pharmazeutische Zusammensetzung, die als wirksamen Bestandteil eine Verbindung mit der Formel (I") oder ihr pharmazeutisch akzeptables Salz enthält:



(I")

worin Q' eine Gruppe mit der Formel:

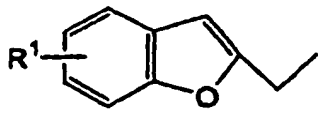
R'-A-B-

worin R' eine Phenylgruppe, Phenoxygruppe oder Benzoylgruppe darstellt, von denen jede mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann,

A eine verbindende Bindung, eine C_{3-6}-Cycloalkylengruppe, eine C_{2-4}-Alkenylengruppe, die mit einer C_{1-3}-Alkylgruppe substituiert sein kann, eine Di-(C_{1-5}alkoxy)methylengruppe oder eine Hydroxyiminomethylengruppe darstellt und

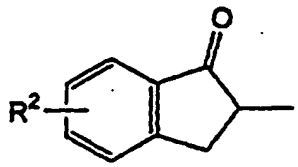
B eine C_{1-6}-Alkylengruppe darstellt, die mit einer Hydroxylgruppe oder einer C_{1-5}-Alkoxygruppe substituiert sein kann;

eine Gruppe mit der Formel:



worin R^1 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt; oder

eine Gruppe mit der Formel:



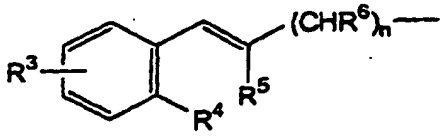
darstellt, worin R^2 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt;

X ein Sauerstoffatom oder eine Methylengruppe darstellt, wobei die Substitution von X für den Benzolring in einer para-Position ist,

E und Y gleich oder verschieden sein können und ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellen,

die gestrichelte Linie die Gegenwart oder Abwesenheit einer Bindung zeigt und R' keine unsubstituierte Phenylgruppe darstellt, wenn X eine Methylengruppe ist, A eine verbindende Bindung ist und B eine unsubstituierte Alkylengruppe ist.

31. Pharmazeutische Zusammensetzung gemäß Anspruch 30, worin in Formel (I") Q' eine Gruppe mit der Formel:



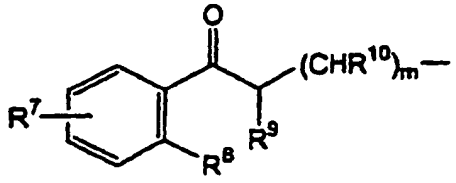
darstellt, worin R^3 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt,

R_4 und R_5 gleich oder verschieden sind und ein Wasserstoffatom oder eine C_{1-3}-Alkylgruppe darstellen oder R^4 und R^5 zusammen -O- darstellen,

R^6 ein Wasserstoffatom, eine Hydroxylgruppe, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe darstellt und

n eine ganze Zahl von 1 bis 6 ist.

32. Pharmazeutische Zusammensetzung gemäß Anspruch 30, worin in Formel (I") Q' eine Gruppe mit der Formel:



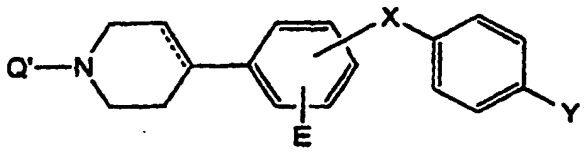
darstellt, worin R^7 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt,

R^8 und R^9 gleich oder verschieden sind und ein Wasserstoffatom oder eine C_{1-5}-Alkylgruppe darstellen oder R^8 und R^9 zusammen eine Methylengruppe darstellen,

R^{10} ein Wasserstoffatom, eine Hydroxylgruppe, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe darstellt und

m eine ganze Zahl von 0 bis 6 ist.

33. Medikament zur Linderung oder Behandlung von Symptomen auf Basis von ischämischen Krankheiten oder Symptomen, die aus Anfällen, Epilepsie und Migräne stammen, das als wirksamen Bestandteil eine Verbindung mit der Formel (II") oder ihr pharmazeutisch akzeptables Salz enthält:



(I")

worin Q' eine Gruppe mit der Formel:

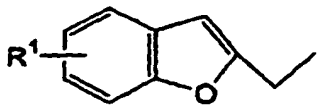
R'-A-B-

worin R' eine Phenylgruppe, Phenoxygruppe oder Benzoylgruppe darstellt, von denen jede mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann,

A eine verbindende Bindung, eine C_{3-6}-Cycloalkylengruppe, eine C_{2-4}-Alkenylengruppe, die mit einer C_{1-3}-Alkylgruppe substituiert sein kann, eine Di-(C_{1-5}alkoxy)methylengruppe oder eine Hydroxyiminomethylengruppe darstellt und

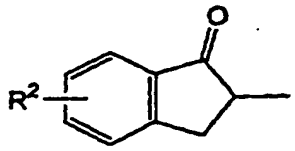
B eine C_{1-6}-Alkylengruppe darstellt, die mit einer Hydroxylgruppe oder einer C_{1-5}-Alkoxygruppe substituiert sein kann;

eine Gruppe mit der Formel:



worin R^1 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt; oder

eine Gruppe mit der Formel:



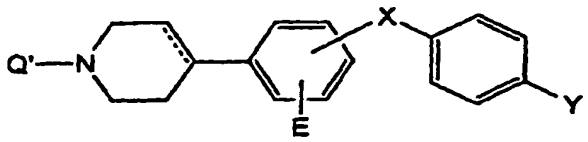
darstellt, worin R^2 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt;

X ein Sauerstoffatom oder eine Methylengruppe darstellt, wobei die Substitution von X für den Benzolring in einer para-Position ist,

E und Y gleich oder verschieden sein können und ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellen,

die gestrichelte Linie die Gegenwart oder Abwesenheit einer Bindung zeigt und R' keine unsubstituierte Phenylgruppe darstellt, wenn X eine Methylengruppe ist, A eine verbindende Bindung ist und B eine unsubstituierte Alkylengruppe ist.

34. Ca^{2+}-Überladungssuppressivum, das als wirksamen Bestandteil eine Verbindung mit der allgemeinen Formel (I") oder ihr pharmazeutisch akzeptables Salz enthält:



(I")

worin Q' eine Gruppe mit der Formel:

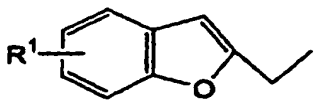
R'-A-B-

worin R' eine Phenylgruppe, Phenoxygruppe oder Benzoylgruppe darstellt, von denen jede mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann,

A eine verbindende Bindung, eine C_{3-6}-Cycloalkylengruppe, eine C_{2-4}-Alkenylengruppe, die mit einer C_{1-3}-Alkylgruppe substituiert sein kann, eine Di-(C_{1-5}alkoxy)methylengruppe oder eine Hydroxyiminomethylengruppe darstellt und

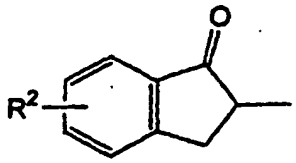
B eine C_{1-6}-Alkylengruppe darstellt, die mit einer Hydroxylgruppe oder einer C_{1-5}-Alkoxygruppe substituiert sein kann;

eine Gruppe mit der Formel:



worin R^1 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt; oder

eine Gruppe mit der Formel:



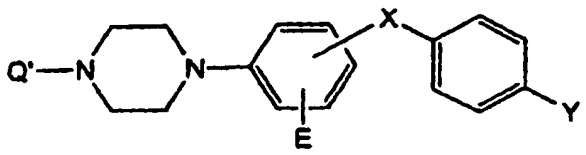
darstellt, worin R^2 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt;

X ein Sauerstoffatom oder eine Methylengruppe darstellt, wobei die Substitution von X für den Benzolring in einer para-Position ist,

E und Y gleich oder verschieden sein können und ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellen,

die gestrichelte Linie die Gegenwart oder Abwesenheit einer Bindung zeigt und R' keine unsubstituierte Phenylgruppe darstellt, wenn X eine Methylengruppe ist, A eine verbindende Bindung ist und B eine unsubstituierte Alkylengruppe ist.

35. Verbindung mit der Formel (I'") oder ihr Salz:



(I'")

worin Q' eine Gruppe mit der Formel:

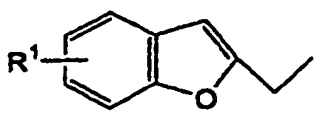
R'-A-B-

worin R' eine Phenylgruppe, Phenoxygruppe oder Benzoylgruppe darstellt, von denen jede mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann,

A eine verbindende Bindung, eine C_{3-6}-Cycloalkylengruppe, eine C_{2-4}-Alkenylengruppe, die mit einer C_{1-3}-Alkylgruppe substituiert sein kann, eine Di-(C_{1-5}alkoxy)methylengruppe oder eine Hydroxyiminomethylengruppe darstellt und

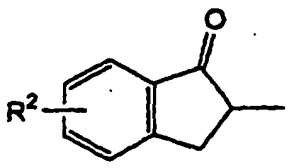
B eine C_{1-6}-Alkylengruppe darstellt, die mit einer Hydroxylgruppe oder einer C_{1-5}-Alkoxygruppe substituiert sein kann;

eine Gruppe mit der Formel:



worin R^1 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt; oder

eine Gruppe mit der Formel:

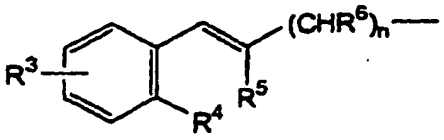


darstellt, worin R^2 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt;

X ein Sauerstoffatom oder eine Methylengruppe darstellt, wobei die Substitution von X für den Benzolring in einer para-Position ist,

E und Y gleich oder verschieden sein können und ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellen.

36. Verbindung oder ihr Salz gemäß Anspruch 35, worin in Formel (I'") Q' eine Gruppe mit der Formel:



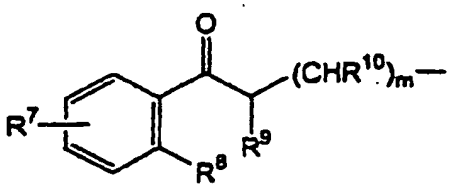
darstellt, worin R^3 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt,

R_4 und R_5 gleich oder verschieden sind und ein Wasserstoffatom oder eine C_{1-3}-Alkylgruppe darstellen oder R^4 und R^5 zusammen -O- darstellen,

R^6 ein Wasserstoffatom, eine Hydroxylgruppe, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe darstellt und

n eine ganze Zahl von 1 bis 6 ist.

37. Verbindung oder ihr Salz gemäß Anspruch 35, worin in Formel (I'") Q' eine Gruppe mit der Formel



darstellt, worin R^7 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt,

R^8 und R^9 gleich oder verschieden sind und ein Wasserstoffatom oder eine C_{1-5}-Alkylgruppe darstellen oder R^8 und R^9 zusammen eine Methylengruppe darstellen,

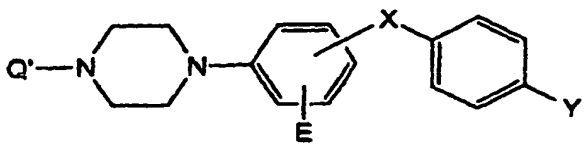
R^{10} ein Wasserstoffatom, eine Hydroxylgruppe, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe darstellt und

m eine ganze Zahl von 0 bis 6 ist.

38. Verbindung oder ihr Salz gemäß Anspruch 35, worin in Formel (I'") R' eine Phenylgruppe darstellt, die mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann, und A eine C_{2-4}-Alkenylengruppe darstellt.

39. Verbindung oder ihr Salz gemäß Anspruch 35, worin in Formel (I'") R' eine Benzoylgruppe darstellt, die mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann, und A eine verbindende Bindung darstellt.

40. Pharmazeutische Zusammensetzung, die als wirksamen Bestandteil eine Verbindung mit der Formel (I'") oder ihr Salz enthält:



(I'")

worin Q' eine Gruppe mit der Formel:

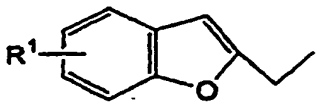
R'-A-B-

worin R' eine Phenylgruppe, Phenoxygruppe oder Benzoylgruppe darstellt, von denen jede mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann,

A eine verbindende Bindung, eine C_{3-6}-Cycloalkylengruppe, eine C_{2-4}-Alkenylengruppe, die mit einer C_{1-3}-Alkylgruppe substituiert sein kann, eine Di-(C_{1-5}alkoxy)methylengruppe oder eine Hydroxyiminomethylengruppe darstellt und

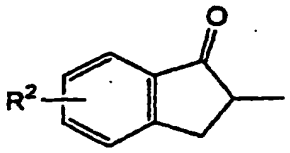
B eine C_{1-6}-Alkylengruppe darstellt, die mit einer Hydroxylgruppe oder einer C_{1-5}-Alkoxygruppe substituiert sein kann;

eine Gruppe mit der Formel:



worin R^1 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt; oder

eine Gruppe mit der Formel:

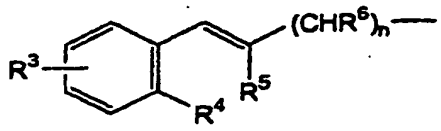


darstellt, worin R^2 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt;

X ein Sauerstoffatom oder eine Methylengruppe darstellt, wobei die Substitution von X für den Benzolring in einer para-Position ist,

E und Y gleich oder verschieden sein können und ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{2-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellen.

41. Pharmazeutische Zusammensetzung gemäß Anspruch 40, worin in Formel (I'") Q' eine Gruppe mit der Formel:



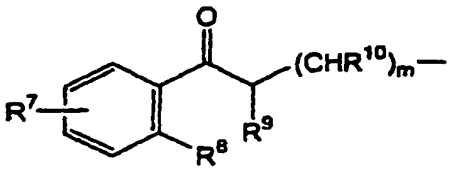
darstellt, worin R^3 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt,

R_4 und R_5 gleich oder verschieden sind und ein Wasserstoffatom oder eine C_{1-3}-Alkylgruppe darstellen oder R^4 und R^5 zusammen -O- darstellen,

R^6 ein Wasserstoffatom, eine Hydroxylgruppe, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe darstellt und

n eine ganze Zahl von 1 bis 6 ist.

42. Pharmazeutische Zusammensetzung gemäß Anspruch 40, worin in Formel (I'") Q' eine Gruppe mit der Formel



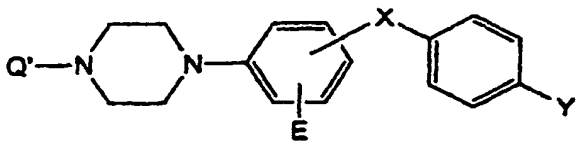
darstellt, worin R^7 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt,

R^8 und R^9 gleich oder verschieden sind und ein Wasserstoffatom oder eine C_{1-5}-Alkylgruppe darstellen oder R^8 und R^9 zusammen eine Methylengruppe darstellen,

R^{10} ein Wasserstoffatom, eine Hydroxylgruppe, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe darstellt und

m eine ganze Zahl von 0 bis 6 ist.

43. Medikament zur Linderung oder Behandlung von Symptomen auf Basis von ischämischen Krankheiten und Symptomen, die aus Anfällen, Epilepsie und Migräne stammen, das als wirksamen Bestandteil eine Verbindung mit der allgemeinen Formel (I'") oder ihr pharmazeutisch akzeptables Salz enthält:



(I'")

worin Q' eine Gruppe mit der Formel:

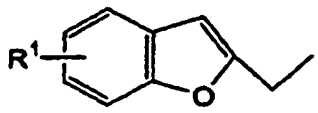
R'-A-B-

worin R' eine Phenylgruppe, Phenoxygruppe oder Benzoylgruppe darstellt, von denen jede mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann,

A eine verbindende Bindung, eine C_{3-6}-Cycloalkylengruppe, eine C_{2-4}-Alkenylengruppe, die mit einer C_{1-3}-Alkylgruppe substituiert sein kann, eine Di-(C_{1-5}alkoxy)methylengruppe oder eine Hydroxyiminomethylengruppe darstellt und

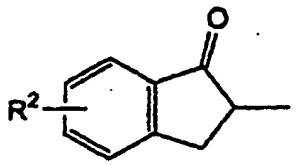
B eine C_{1-6}-Alkylengruppe darstellt, die mit einer Hydroxylgruppe oder einer C_{1-5}-Alkoxygruppe substituiert sein kann;

eine Gruppe mit der Formel:



worin R^1 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt; oder

eine Gruppe mit der Formel:

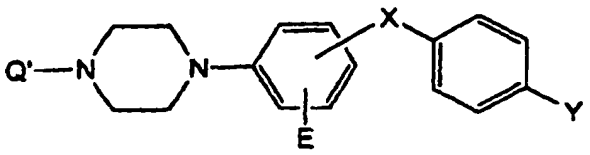


darstellt, worin R^2 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt;

X ein Sauerstoffatom oder eine Methylengruppe darstellt, wobei die Substitution von X für den Benzolring in einer para-Position ist,

E und Y gleich oder verschieden sein können und ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellen.

44. Ca^{2+}-Überladungssuppressivum, das als wirksamen Bestandteil eine Verbindung mit der Formel (I'") oder ihr pharmazeutisch akzeptables Salz enthält:



(I'")

worin Q' eine Gruppe mit der Formel:

R'-A-B-

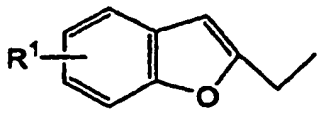
worin R' eine Phenylgruppe, Phenoxygruppe oder Benzoylgruppe darstellt, von denen jede mit einem Halogenatom, einer Hydroxylgruppe, einer C_{1-5}-Alkoxygruppe oder einer C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, substituiert sein kann,

A eine verbindende Bindung, eine C_{3-6}-Cycloalkylengruppe, eine C_{2-4}-Alkenylengruppe, die mit einer C_{1-3}-Alkylgruppe substituiert sein kann, eine Di-(C_{1-5}alkoxy)methylengruppe oder eine Hydroxyiminomethylengruppe darstellt und

B eine C_{1-6}-Alkylengruppe darstellt, die mit einer Hydroxylgruppe oder einer C_{1-5}-Alkoxygruppe substituiert

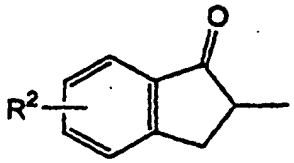
sein kann;

eine Gruppe mit der Formel:



worin R^1 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt; oder

eine Gruppe mit der Formel:

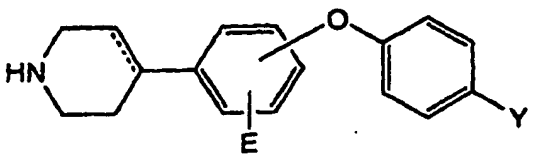


darstellt, worin R^2 ein Wasserstoffatom, ein Halogenatom, eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, eine C_{1-5}-Alkoxygruppe oder eine Hydroxylgruppe darstellt;

X ein Sauerstoffatom oder eine Methylengruppe darstellt, wobei die Substitution von X für den Benzolring in einer para-Position ist,

E und Y gleich oder verschieden sein können und ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellen.

45. Verbindung mit der allgemeinen Formel (IIa) oder ihr Salz:

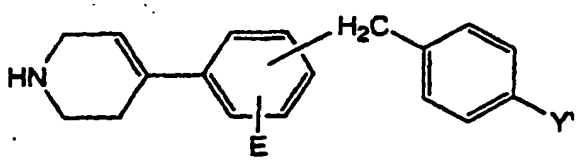


(IIa)

worin E und Y gleich oder verschieden sein können und ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe darstellen, die mit einem Halogenatom substituiert sein kann, darstellen,

die gestrichelte Linie die Gegenwart und Abwesenheit einer Bindung zeigt und die Substitution des Benzolrings, der mit dem Piperidinring oder dem Tetrahydropyridinring und der Gruppe $-OC_6H_4Y$ bindet, in einer para-Position ist.

46. Verbindung mit der Formel (IIb) oder ihr Salz:

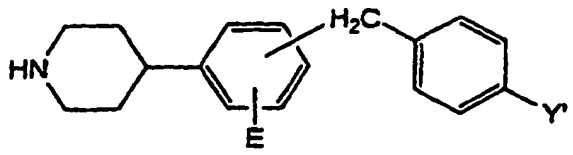


(IIb)

worin E eine Wasserstoffgruppe, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellt, Y' eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellt, und

die Substitution des Benzolrings, der mit dem Tetrahydropyridinring und der Gruppe $-CH_2C_6H_4Y'$ bindet, in einer para-Position ist.

47. Verbindung mit der Formel (IIc) oder ihr Salz:

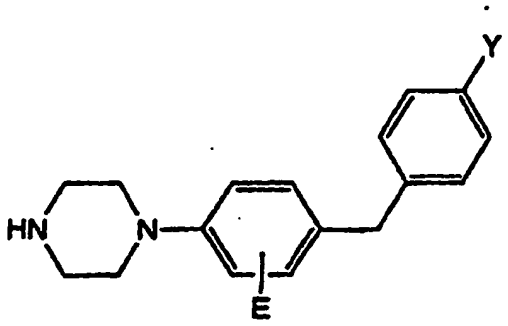


(IIc)

worin E ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellt, Y' eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellt, und

die Substitution des Benzolrings, der mit dem Piperidinring und der Gruppe $-CH_2C_6H_4Y'$ bindet, in einer para-Position ist.

48. Verbindung mit der Formel (IIIa) oder ihr Salz:

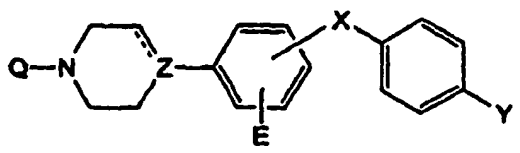


(IIIa)

worin E und Y gleich oder verschieden sein können und ein Wasserstoffatom, eine Hydroxylgruppe, ein Halogenatom, eine C_{1-5}-Alkoxygruppe oder eine C_{1-5}-Alkylgruppe, die mit einem Halogenatom substituiert sein kann, darstellen.

Revendications

1. Médicament pour soulager ou traiter des symptômes basés sur des maladies ischémiques ou des symptômes dérivant de crises, d'épilepsie et de migraine, contenant, à titre d'ingrédient efficace, un composé de formule (I) ou son sel acceptable en pharmacie :



(I)

où Q représente un groupe de formule :

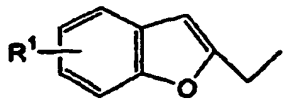
R-A-B-

dans laquelle R représente un atome d'hydrogène ou un groupe phényle, un groupe phénoxy ou un groupe benzoyle, chacun pouvant être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

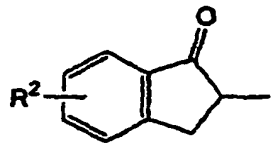
A représente une liaison de connexion, un groupe cycloalkylène en C_3 à C_6, un groupe alcénylène en C_2 à C_4 qui peut être substitué par un groupe alkyle en C_1 à C_3, un groupe di (alcoxy en C_1 à C_5)méthylène, ou un groupe hydroxyiminométhylène, et

B représente un groupe alkylène en C_1 à C_6 qui peut être substitué par un groupe hydroxyle ou un groupe alcoxy en C_1 à C_5 ;

un groupe de formule :



dans laquelle R^1 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ; ou un groupe de formule :



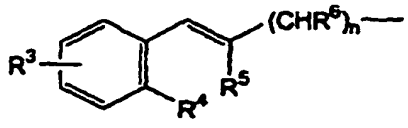
dans laquelle R^2 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ;

X représente un atome d'oxygène ou un groupe méthylène, la substitution de X pour le cycle benzène étant en position para,

E et Y peuvent être mutuellement identiques ou différents, et représentent un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

la ligne de tirets montre la présence ou l'absence d'une liaison, quand ladite ligne de tirets indique la présence d'une liaison, Z représente un atome de carbone, et quand ladite ligne de tirets montre l'absence d'une liaison, Z représente CH ou un atome d'azote.

2. Médicament pour soulager ou traiter des symptômes basés sur des maladies ischémiques ou des symptômes dérivant de crises, d'épilepsie et de migraine, selon la revendication 1, dans lequel, dans la formule (I), Q représente un groupe de formule :

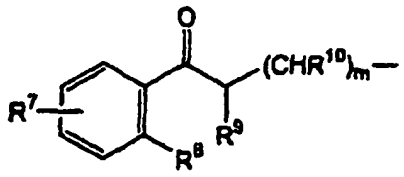


dans laquelle R^3 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle,

R^4 et R^5 sont mutuellement identiques ou différents et représentent un atome d'hydrogène ou un groupe alkyle en C_1 à C_3, ou bien R^4 et R^5 sont pris ensemble pour représenter -O-,

R^6 représente un atome d'hydrogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5, et n est un entier de 1 à 6.

3. Médicament pour soulager ou traiter des symptômes basés sur des maladies ischémiques ou des symptômes dérivant de crises, d'épilepsie et de migraine, selon la revendication 1, dans lequel, dans la formule (I), Q représente un groupe de formule :



dans laquelle R^7 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle,

R^8 et R^9 sont mutuellement identiques ou différents et représentent un atome d'hydrogène ou un groupe alkyle en C_1 à C_5, ou bien R^8 et R^9 sont pris ensemble pour représenter un groupe méthylène,

R^{10} représente un atome d'hydrogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5, et m est un entier de 0 à 6.

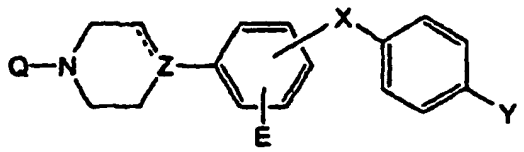
4. Médicament pour soulager ou traiter des symptômes basés sur des maladies ischémiques ou des symptômes dérivant de crises, d'épilepsie et de migraine, selon la revendication 1, dans lequel, dans la formule (I), R représente un groupe phényle qui peut être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, et A représente un groupe alcénylène en C_2 à C_4.

5. Médicament pour soulager ou traiter des symptômes basés sur des maladies ischémiques ou des symptômes dérivant de crises, d'épilepsie et de migraine, selon la revendication 1, dans lequel, dans la formule (I), R représente un groupe benzoyle qui peut être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, et A représente une liaison de connexion.

6. Médicament pour soulager ou traiter des symptômes basés sur des maladies ischémiques ou des symptômes dérivant de crises, d'épilepsie et de migraine, selon la revendication 1, dans lequel, dans la formule (I), R représente un groupe phényle qui peut être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, A représente une liaison de connexion, et B représente un groupe diméthylène qui est substitué par un groupe hydroxyle.

7. Médicament pour soulager ou traiter des symptômes basés sur des maladies ischémiques ou des symptômes dérivant de crises, d'épilepsie et de migraine, selon la revendication 1, dans lequel, dans la formule (I), R représente un groupe phénoxy qui peut être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, A représente une liaison de connexion, et B représente un groupe triméthylène qui est substitué par un groupe hydroxyle.

8. Utilisation, pour la fabrication d'un médicament pour soulager ou traiter des symptômes basés sur des maladies ischémiques ou des symptômes dérivant de crises, d'épilepsie et de migraine, d'un composé de formule (I) ou de son sel acceptable en pharmacie :



(I)

où Q représente un groupe de formule :

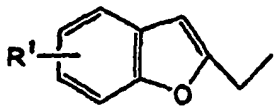
R-A-B-

dans laquelle R représente un atome d'hydrogène ou un groupe phényle, un groupe phénoxy ou un groupe benzoyle, chacun pouvant être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

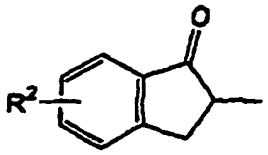
A représente une liaison de connexion, un groupe cycloalkylène en C_3 à C_6, un groupe alcénylène en C_2 à C_4 qui peut être substitué par un groupe alkyle en C_1 à C_3, un groupe di (alcoxy en C_1 à C_5)méthylène, ou un groupe hydroxyiminométhylène, et

B représente un groupe alkylène en C_1 à C_6 qui peut être substitué par un groupe hydroxyle ou un groupe alcoxy en C_1 à C_5 ;

un groupe de formule :



dans laquelle R^1 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en Ci à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ; ou
un groupe de formule :



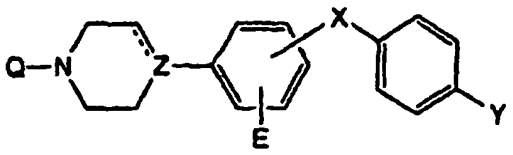
dans laquelle R^2 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ;

X représente un atome d'oxygène ou un groupe méthylène, la substitution de X pour le cycle benzène étant en position para,

E et Y peuvent être mutuellement identiques ou différents, et représentent un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en Ci à C_5 qui peut être substitué par un atome d'halogène,

la ligne de tirets montre la présence ou l'absence d'une liaison, quand ladite ligne de tirets indique la présence d'une liaison, Z représente un atome de carbone, et quand ladite ligne de tirets montre l'absence d'une liaison, Z représente CH ou un atome d'azote.

9. Suppresseur de surcharge en Ca^{2+} contenant, à titre d'ingrédient actif, un composé de formule (I) ou son sel acceptable en pharmacie :



(I)

où Q représente un groupe de formule :

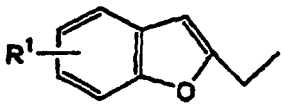
R-A-B-

dans laquelle R représente un atome d'hydrogène ou un groupe phényle, un groupe phénoxy ou un groupe benzoyle, chacun pouvant être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

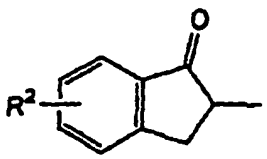
A représente une liaison de connexion, un groupe cycloalkylène en C_3 à C_6, un groupe alcénylène en C_2 à C_4 qui peut être substitué par un groupe alkyle en C_1 à C_3, un groupe di(alcoxy en C_1 à C_5)méthylène, ou un groupe hydroxyiminométhylène, et

B représente un groupe alkylène en C_1 à C_6 qui peut être substitué par un groupe hydroxyle ou un groupe alcoxy en C_1 à C_5 ;

un groupe de formule :



dans laquelle R^1 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ; ou un groupe de formule :



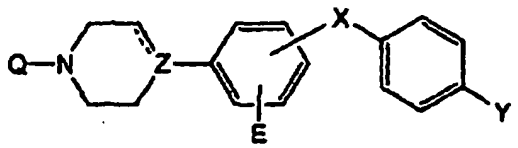
dans laquelle R^2 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ;

X représente un atome d'oxygène ou un groupe méthylène, la substitution de X pour le cycle benzène étant en position para,

E et Y peuvent être mutuellement identiques ou différents, et représentent un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

la ligne de tirets montre la présence ou l'absence d'une liaison, quand ladite ligne de tirets indique la présence d'une liaison, Z représente un atome de carbone, et quand ladite ligne de tirets montre l'absence d'une liaison, Z représente CH ou un atome d'azote.

10. Utilisation, pour la fabrication d'un suppresseur de surcharge en Ca^{2+}, d'un composé de formule (I) ou de son sel acceptable en pharmacie :



(I)

où Q représente un groupe de formule :

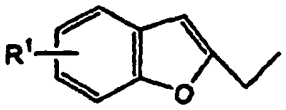
R-A-B-

dans laquelle R représente un atome d'hydrogène ou un groupe phényle, un groupe phénoxy ou un groupe benzoyle, chacun pouvant être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

A représente une liaison de connexion, un groupe cycloalkylène en C_3 à C_6, un groupe alcénylène en C_2 à C_4 qui peut être substitué par un groupe alkyle en C_1 à C_3, un groupe di (alcoxy en C_1 à C_5)méthylène, ou un groupe hydroxyiminométhylène, et

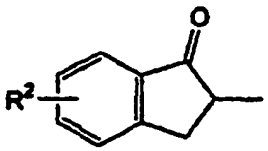
B représente un groupe alkylène en C_1 à C_6 qui peut être substitué par un groupe hydroxyle ou un groupe alcoxy en C_1 à C_5 ;

un groupe de formule :



dans laquelle R^1 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ; ou

un groupe de formule :



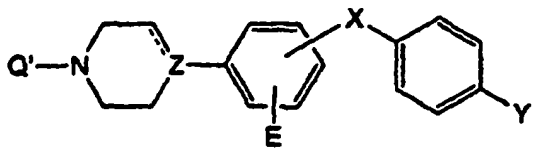
dans laquelle R^2 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ;

X représente un atome d'oxygène ou un groupe méthylène, la substitution de X pour le cycle benzène étant en position para,

E et Y peuvent être mutuellement identiques ou différents, et représentent un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

la ligne de tirets montre la présence ou l'absence d'une liaison, quand ladite ligne de tirets indique la présence d'une liaison, Z représente un atome de carbone, et quand ladite ligne de tirets montre l'absence d'une liaison, Z représente CH ou un atome d'azote.

11. Composé de formule (I') ou ses sels :



(I')

où Q' représente un groupe de formule :

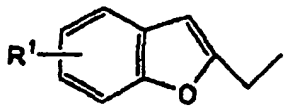
R'-A-B-

dans laquelle R' représente un groupe phényle, un groupe phénoxy ou un groupe benzoyle, chacun pouvant être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

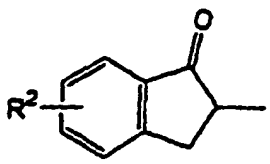
A représente une liaison de connexion, un groupe cycloalkylène en C_3 à C_6, un groupe alcénylène en C_2 à C_4 qui peut être substitué par un groupe alkyle en C_1 à C_3, un groupe di(alcoxy en C_1 à C_5)méthylène, ou un groupe hydroxyiminométhylène, et

B représente un groupe alkylène en C_1 à C_6 qui peut être substitué par un groupe hydroxyle ou un groupe alcoxy en C_1 à C_5 ;

un groupe de formule :



dans laquelle R^1 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ; ou un groupe de formule :



dans laquelle R^2 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ;

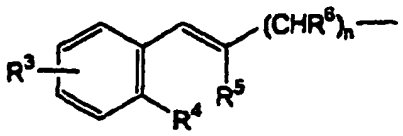
X représente un atome d'oxygène ou un groupe méthylène, la substitution de X pour le cycle benzène étant en position para,

E et Y peuvent être mutuellement identiques ou différents, et représentent un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

la ligne de tirets montre la présence ou l'absence d'une liaison, quand ladite ligne de tirets indique la présence d'une liaison, Z représente un atome de carbone, et quand ladite ligne de tirets montre l'absence d'une liaison, Z représente CH ou un atome d'azote,

quand Z est un atome de carbone ou CH, X est un groupe méthylène, A est une liaison de connexion, et B est un groupe alkylène non substitué, R' ne représente pas un groupe phényle non substitué.

12. Composé ou son sel selon la revendication 11, dans lequel, dans la formule (I'), Q' représente un groupe de formule :

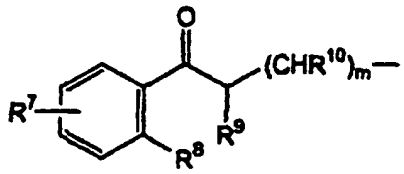


dans laquelle R^3 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle,

R^4 et R^5 sont mutuellement identiques ou différents et représentent un atome d'hydrogène ou un groupe alkyle en C_1 à C_3, ou bien R^4 et R^5 sont pris ensemble pour représenter -O-,

R^6 représente un atome d'hydrogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5, et n est un entier de 1 à 6.

13. Composé ou son sel selon la revendication 11, dans lequel, dans la formule (I'), Q' représente un groupe de formule :



dans laquelle R^7 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle,

R^8 et R^9 sont mutuellement identiques ou différents et représentent un atome d'hydrogène ou un groupe alkyle en C_1 à C_5, ou bien R^8 et R^9 sont pris ensemble pour représenter un groupe méthylène,

R^{10} représente un atome d'hydrogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5, et m est un entier de 0 à 6.

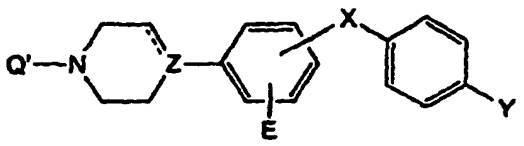
14. Composé ou son sel selon la revendication 11, dans lequel, dans la formule (I'), R' représente un groupe phényle qui peut être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, et A représente un groupe alcénylène en C_2 à C_4.

15. Composé ou son sel selon la revendication 11, dans lequel, dans la formule (I'), R' représente un groupe benzoyle qui peut être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, et A représente une liaison de connexion.

16. Composé ou son sel selon la revendication 11, dans lequel, dans la formule (I'), R' représente un groupe phényle qui peut être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, A représente une liaison de connexion, et B représente un groupe diméthylène qui est substitué par un groupe hydroxyle.

17. Composé ou son sel selon la revendication 11, dans lequel, dans la formule (I'), R' représente un groupe phénoxy qui peut être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, A représente une liaison de connexion, et B représente un groupe triméthylène qui est substitué par un groupe hydroxyle.

18. Composition pharmaceutique contenant, à titre d'ingrédient actif, un composé de formule (I') ou son sel acceptable en pharmacie :



(I')

où Q' représente un groupe de formule :

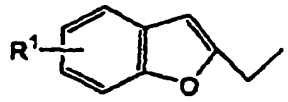
R'-A-B-

dans laquelle R' représente un groupe phényle, un groupe phénoxy ou un groupe benzoyle, chacun pouvant être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

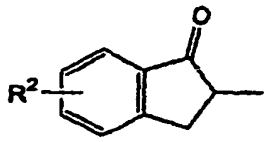
A représente une liaison de connexion, un groupe cycloalkylène en C_3 à C_6, un groupe alcénylène en C_2 à C_4 qui peut être substitué par un groupe alkyle en C_1 à C_3, un groupe di (alcoxy en C_1 à C_5)méthylène, ou un groupe hydroxyiminométhylène, et

B représente un groupe alkylène en C_1 à C_6 qui peut être substitué par un groupe hydroxyle ou un groupe alcoxy en C_1 à C_5 ;

un groupe de formule :



dans laquelle R^1 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ; ou un groupe de formule :



dans laquelle R^2 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ;

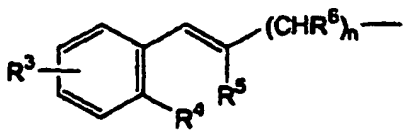
X représente un atome d'oxygène ou un groupe méthylène, la substitution de X pour le cycle benzène étant en position para,

E et Y peuvent être mutuellement identiques ou différents, et représentent un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

la ligne de tirets montre la présence ou l'absence d'une liaison, quand ladite ligne de tirets indique la présence d'une liaison, Z représente un atome de carbone, et quand ladite ligne de tirets montre l'absence d'une liaison, Z représente CH ou un atome d'azote,

quand Z est un atome de carbone ou CH, X est un groupe méthylène, A est une liaison de connexion, et B est un groupe alkylène non substitué, R' ne représente pas un groupe phényle non substitué.

19. Composition pharmaceutique selon la revendication 18, dans laquelle, dans la formule (I'), Q' représente un groupe de formule :

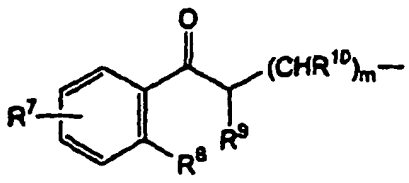


dans laquelle R^3 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle,

R^4 et R^5 sont mutuellement identiques ou différents et représentent un atome d'hydrogène ou un groupe alkyle en C_1 à C_3, ou bien R^4 et R^5 sont pris ensemble pour représenter -O-,

R^6 représente un atome d'hydrogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5, et n est un entier de 1 à 6.

20. Composition pharmaceutique selon la revendication 18, dans laquelle, dans la formule (I'), Q' représente un groupe de formule :

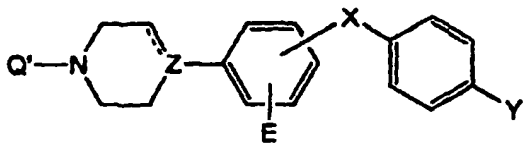


dans laquelle R^7 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle,

R^8 et R^9 sont mutuellement identiques ou différents et représentent un atome d'hydrogène ou un groupe alkyle en C_1 à C_5, ou bien R^8 et R^9 sont pris ensemble pour représenter un groupe méthylène,

R^{10} représente un atome d'hydrogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5, et m est un entier de 0 à 6.

21. Médicament pour soulager ou traiter des symptômes basés sur des maladies ischémiques ou des symptômes dérivant de crises, d'épilepsie et de migraine, contenant, à titre d'ingrédient efficace, un composé de formule (I') ou son sel acceptable en pharmacie :



(I')

où Q' représente un groupe de formule :

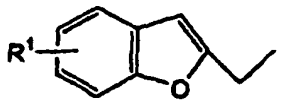
R'-A-B-

dans laquelle R' représente un groupe phényle, un groupe phénoxy ou un groupe benzoyle, chacun pouvant être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

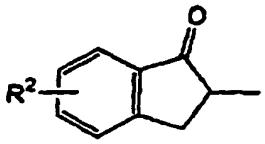
A représente une liaison de connexion, un groupe cycloalkylène en C_3 à C_6, un groupe alcénylène en C_2 à C_4 qui peut être substitué par un groupe alkyle en C_1 à C_3, un groupe di(alcoxy en C_1 à C_5)méthylène, ou un groupe hydroxyiminométhylène, et

B représente un groupe alkylène en C_1 à C_6 qui peut être substitué par un groupe hydroxyle ou un groupe alcoxy en C_1 à C_5 ;

un groupe de formule :



dans laquelle R^1 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ; ou un groupe de formule :



dans laquelle R^2 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ;

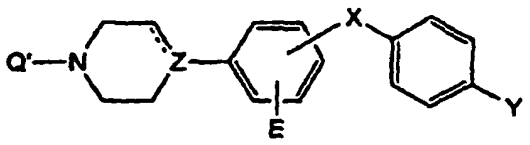
X représente un atome d'oxygène ou un groupe méthylène, la substitution de X pour le cycle benzène étant en position para,

E et Y peuvent être mutuellement identiques ou différents, et représentent un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

la ligne de tirets montre la présence ou l'absence d'une liaison, quand ladite ligne de tirets indique la présence d'une liaison, Z représente un atome de carbone, et quand ladite ligne de tirets montre l'absence d'une liaison, Z représente CH ou un atome d'azote,

quand Z est un atome de carbone ou CH, X est un groupe méthylène, A est une liaison de connexion, et B est un groupe alkylène non substitué, R' ne représente pas un groupe phényle non substitué.

22. Suppresseur de surcharge en Ca^{2+} contenant, à titre d'ingrédient actif, un composé de formule (I') ou son sel acceptable en pharmacie :



(I')

où Q' représente un groupe de formule :

R'-A-B-

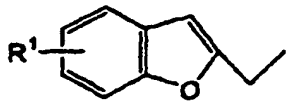
dans laquelle R' représente un groupe phényle, un groupe phénoxy ou un groupe benzoyle, chacun pouvant être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

A représente une liaison de connexion, un groupe cycloalkylène en C_3 à C_6, un groupe alcénylène en C_2 à

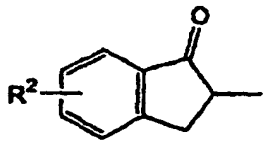
C_4 qui peut être substitué par un groupe alkyle en C_1 à C_3, un groupe di (alcoxy en C_1 à C_5)méthylène, ou un groupe hydroxyiminométhylène, et

B représente un groupe alkylène en C_1 à C_6 qui peut être substitué par un groupe hydroxyle ou un groupe alcoxy en C_1 à C_5 ;

un groupe de formule :



dans laquelle R^1 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ; ou un groupe de formule :



dans laquelle R^2 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ;

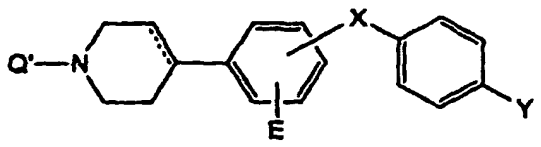
X représente un atome d'oxygène ou un groupe méthylène, la substitution de X pour le cycle benzène étant en position para,

E et Y peuvent être mutuellement identiques ou différents, et représentent un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

la ligne de tirets montre la présence ou l'absence d'une liaison, quand ladite ligne de tirets indique la présence d'une liaison, Z représente un atome de carbone, et quand ladite ligne de tirets montre l'absence d'une liaison, Z représente CH ou un atome d'azote,

quand Z est un atome de carbone ou CH, X est un groupe méthylène, A est une liaison de connexion, et B est un groupe alkylène non substitué, R' ne représente pas un groupe phényle non substitué.

23. Composé de formule (I") ou ses sels :



(I")

où Q' représente un groupe de formule :

R'-A-B-

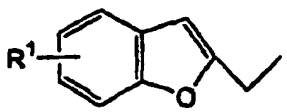
dans laquelle R' représente un groupe phényle, un groupe phénoxy ou un groupe benzoyle, chacun pouvant être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle

en C_1 à C_5 qui peut être substitué par un atome d'halogène,

A représente une liaison de connexion, un groupe cycloalkylène en C_3 à C_6, un groupe alcénylène en C_2 à C_4 qui peut être substitué par un groupe alkyle en C_1 à C_3, un groupe di (alcoxy en C_1 à C_5)méthylène, ou un groupe hydroxyiminométhylène, et

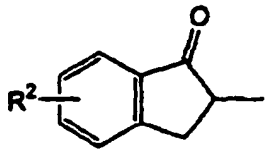
B représente un groupe alkylène en Ci à C_6 qui peut être substitué par un groupe hydroxyle ou un groupe alcoxy en C_1 à C_5 ;

un groupe de formule :



dans laquelle R^1 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ; ou

un groupe de formule :



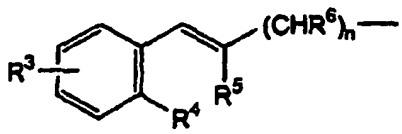
dans laquelle R^2 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ;

X représente un atome d'oxygène ou un groupe méthylène, la substitution de X pour le cycle benzène étant en position para,

E et Y peuvent être mutuellement identiques ou différents, et représentent un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

la ligne de tirets montre la présence ou l'absence d'une liaison, et quand X est un groupe méthylène, A est une liaison de connexion et B est un groupe alkylène non substitué, R' ne représente pas un groupe phényle non substitué.

24. Composé ou son sel selon la revendication 23, dans lequel, dans la formule (I"), Q' représente un groupe de formule :



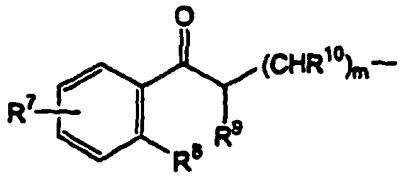
dans laquelle R^3 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle,

R^4 et R^5 sont mutuellement identiques ou différents et représentent un atome d'hydrogène ou un groupe alkyle en C_1 à C_3, ou bien R^4 et R^5 sont pris ensemble pour représenter -O-,

R^6 représente un atome d'hydrogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5, et

n est un entier de 1 à 6.

25. Composé ou son sel selon la revendication 23, dans lequel, dans la formule (I"), Q' représente un groupe de formule :



dans laquelle R^7 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle,

R^8 et R^9 sont mutuellement identiques ou différents et représentent un atome d'hydrogène ou un groupe alkyle en C_1 à C_5, ou bien R^8 et R^9 sont pris ensemble pour représenter un groupe méthylène,

R^{10} représente un atome d'hydrogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5, et m est un entier de 0 à 6.

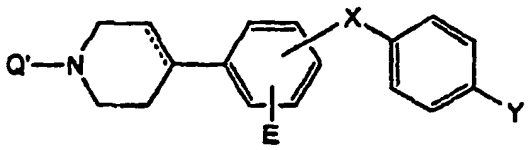
26. Composé ou son sel selon la revendication 23, dans lequel, dans la formule (I"), R' représente un groupe phényle qui peut être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, et A représente un groupe alcénylène en C_2 à C_4.

27. Composé ou son sel selon la revendication 23, dans lequel, dans la formule (I"), R' représente un groupe benzoyle qui peut être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, et A représente une liaison de connexion.

28. Composé ou son sel selon la revendication 23, dans lequel, dans la formule (I"), R' représente un groupe phényle qui peut être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, A représente une liaison de connexion, et B représente un groupe diméthylène qui est substitué par un groupe hydroxyle.

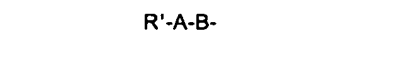
29. Composé ou son sel selon la revendication 23, dans lequel, dans la formule (I"), R' représente un groupe phénoxy qui peut être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, A représente une liaison de connexion, et B représente un groupe triméthylène qui est substitué par un groupe hydroxyle.

30. Composition pharmaceutique contenant, à titre d'ingrédient actif, un composé de formule (I") ou son sel acceptable en pharmacie :



(I")

où Q' représente un groupe de formule :



R'-A-B-

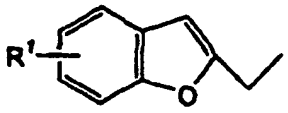
dans laquelle R' représente un groupe phényle, un groupe phénoxy ou un groupe benzoyle, chacun pouvant être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

A représente une liaison de connexion, un groupe cycloalkylène en C_3 à C_6, un groupe alcénylène en C_2 à

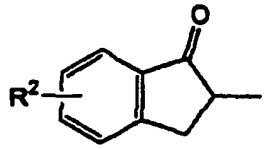
C_4 qui peut être substitué par un groupe alkyle en C_1 à C_3, un groupe di(alcoxy en C_1 à C_5)méthylène, ou un groupe hydroxyiminométhylène, et

B représente un groupe alkylène en C_1 à C_6 qui peut être substitué par un groupe hydroxyle ou un groupe alcoxy en C_1 à C_5 ;

un groupe de formule :



dans laquelle R^1 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ; ou un groupe de formule :



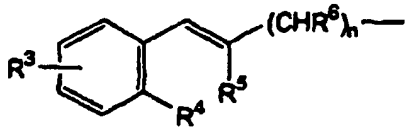
dans laquelle R^2 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ;

X représente un atome d'oxygène ou un groupe méthylène, la substitution de X pour le cycle benzène étant en position para,

E et Y peuvent être mutuellement identiques ou différents, et représentent un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

la ligne de tirets montre la présence ou l'absence d'une liaison, et quand X est un groupe méthylène, A est une liaison de connexion et B est un groupe alkylène non substitué, R' ne représente pas un groupe phényle non substitué.

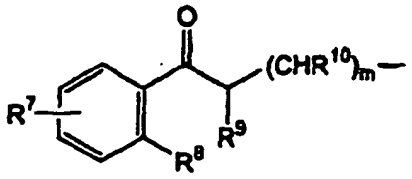
31. Composition pharmaceutique selon la revendication 30, dans laquelle, dans la formule (I"), Q' représente un groupe de formule :



dans laquelle R^3 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle,

R^4 et R^5 sont mutuellement identiques ou différents et représentent un atome d'hydrogène ou un groupe alkyle en C_1 à C_3, ou bien R^4 et R^5 sont pris ensemble pour représenter -O-, R^6 représente un atome d'hydrogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5, et n est un entier de 1 à 6.

32. Composition pharmaceutique selon la revendication 30, dans laquelle, dans la formule (I"), Q' représente un groupe de formule :

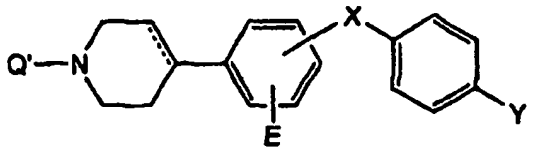


dans laquelle R^7 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle,

R^8 et R^9 sont mutuellement identiques ou différents et représentent un atome d'hydrogène ou un groupe alkyle en C_1 à C_5, ou bien R^8 et R^9 sont pris ensemble pour représenter un groupe méthylène,

R^{10} représente un atome d'hydrogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5, et m est un entier de 0 à 6.

33. Médicament pour soulager ou traiter des symptômes basés sur des maladies ischémiques ou des symptômes dérivant de crises, d'épilepsie et de migraine, contenant, à titre d'ingrédient efficace, un composé de formule (I") ou son sel acceptable en pharmacie :



(I")

où Q' représente un groupe de formule :

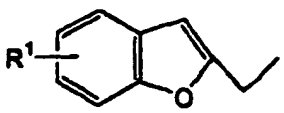
R'-A-B-

dans laquelle R' représente un groupe phényle, un groupe phénoxy ou un groupe benzoyle, chacun pouvant être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

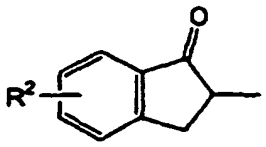
A représente une liaison de connexion, un groupe cycloalkylène en C_3 à C_6, un groupe alcénylène en C_2 à C_4 qui peut être substitué par un groupe alkyle en C_1 à C_3, un groupe di (alcoxy en C_1 à C_5)méthylène, ou un groupe hydroxyiminométhylène, et

B représente un groupe alkylène en C_1 à C_6 qui peut être substitué par un groupe hydroxyle ou un groupe alcoxy en C_1 à C_5 ;

un groupe de formule :



dans laquelle R^1 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ; ou un groupe de formule :



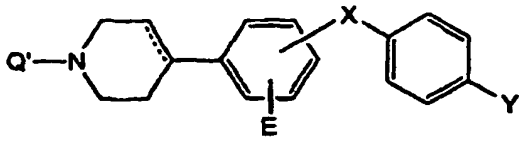
dans laquelle R^2 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ;

X représente un atome d'oxygène ou un groupe méthylène, la substitution de X pour le cycle benzène étant en position para,

E et Y peuvent être mutuellement identiques ou différents, et représentent un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

la ligne de tirets montre la présence ou l'absence d'une liaison, et quand X est un groupe méthylène, A est une liaison de connexion et B est un groupe alkylène non substitué, R' ne représente pas un groupe phényle non substitué.

34. Suppresseur de surcharge en Ca^{2+} contenant, à titre d'ingrédient actif, un composé de formule (I") ou son sel acceptable en pharmacie :



(I")

où Q' représente un groupe de formule :

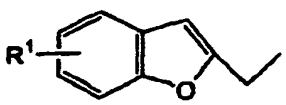
R'-A-B-

dans laquelle R' représente un groupe phényle, un groupe phénoxy ou un groupe benzoyle, chacun pouvant être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

A représente une liaison de connexion, un groupe cycloalkylène en C_3 à C_6, un groupe alcénylène en C_2 à C_4 qui peut être substitué par un groupe alkyle en C_1 à C_3, un groupe di (alcoxy en C_1 à C_5)méthylène, ou un groupe hydroxyiminométhylène, et

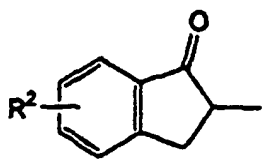
B représente un groupe alkylène en C_1 à C_6 qui peut être substitué par un groupe hydroxyle ou un groupe alcoxy en C_1 à C_5 ;

un groupe de formule :



dans laquelle R^1 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut

être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ; ou un groupe de formule :



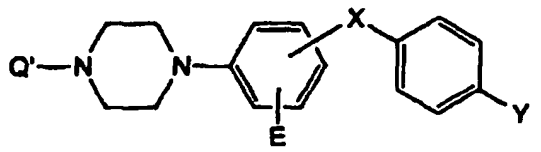
dans laquelle R^2 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ;

X représente un atome d'oxygène ou un groupe méthylène, la substitution de X pour le cycle benzène étant en position para,

E et Y peuvent être mutuellement identiques ou différents, et représentent un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

la ligne de tirets montre la présence ou l'absence d'une liaison, et quand X est un groupe méthylène, A est une liaison de connexion et B est un groupe alkylène non substitué, R' ne représente pas un groupe phényle non substitué.

35. Composé de formule (I'''') ou son sel :



(I'''')

où Q' représente un groupe de formule :

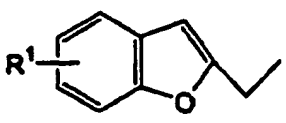
R'-A-B-

dans laquelle R' représente un groupe phényle, un groupe phénoxy ou un groupe benzoyle, chacun pouvant être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

A représente une liaison de connexion, un groupe cycloalkylène en C_3 à C_6, un groupe alcénylène en C_2 à C_4 qui peut être substitué par un groupe alkyle en C_1 à C_3, un groupe di (alcoxy en C_1 à C_5)méthylène, ou un groupe hydroxyiminométhylène, et

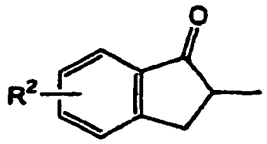
B représente un groupe alkylène en C_1 à C_6 qui peut être substitué par un groupe hydroxyle ou un groupe alcoxy en C_1 à C_5 ;

un groupe de formule :



dans laquelle R^1 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ; ou

un groupe de formule :

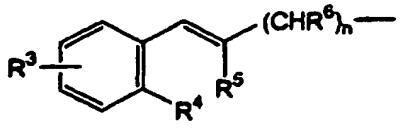


dans laquelle R^2 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ;

X représente un atome d'oxygène ou un groupe méthylène, la substitution de X pour le cycle benzène étant en position para,

E et Y peuvent être mutuellement identiques ou différents, et représentent un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène.

36. Composé ou son sel selon la revendication 35, dans lequel, dans la formule (I'''), Q' représente un groupe de formule :

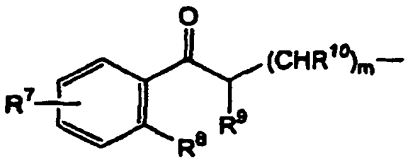


dans laquelle R^3 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle,

R^4 et R^5 sont mutuellement identiques ou différents et représentent un atome d'hydrogène ou un groupe alkyle en C_1 à C_3, ou bien R^4 et R^5 sont pris ensemble pour représenter -O-,

R^6 représente un atome d'hydrogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5, et n est un entier de 1 à 6.

37. Composé ou son sel selon la revendication 35, dans lequel, dans la formule (I'''), Q' représente un groupe de formule :



dans laquelle R^7 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle,

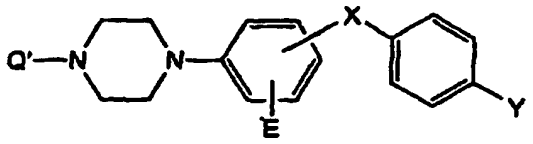
R^8 et R^9 sont mutuellement identiques ou différents et représentent un atome d'hydrogène ou un groupe alkyle en C_1 à C_5, ou bien R^8 et R^9 sont pris ensemble pour représenter un groupe méthylène,

R^{10} représente un atome d'hydrogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5, et m est un entier de 0 à 6.

38. Composé ou son sel selon la revendication 35, dans lequel, dans la formule (I'''), R' représente un groupe phényle qui peut être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, et A représente un groupe alcénylène en C_2 à C_4.

39. Composé ou son sel selon la revendication 35, dans lequel, dans la formule (I'''), R' représente un groupe benzoyle qui peut être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, et A représente une liaison de connexion.

40. Composition pharmaceutique contenant, à titre d'ingrédient actif, un composé de formule (I''') ou son sel acceptable en pharmacie :



(I''')

où Q' représente un groupe de formule :

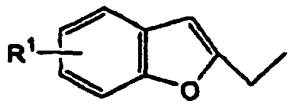
R'-A-B-

dans laquelle R' représente un groupe phényle, un groupe phénoxy ou un groupe benzoyle, chacun pouvant être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

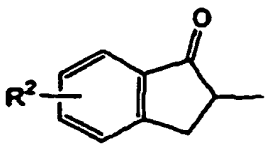
A représente une liaison de connexion, un groupe cycloalkylène en C_3 à C_6, un groupe alcénylène en C_2 à C_4 qui peut être substitué par un groupe alkyle en C_1 à C_3, un groupe di (alcoxy en C_1 à C_5)méthylène, ou un groupe hydroxyiminométhylène, et

B représente un groupe alkylène en C_1 à C_6 qui peut être substitué par un groupe hydroxyle ou un groupe alcoxy en C_1 à C_5 ;

un groupe de formule :



dans laquelle R^1 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ; ou
un groupe de formule :



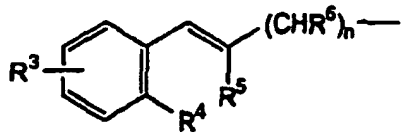
dans laquelle R^2 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ;

X représente un atome d'oxygène ou un groupe méthylène, la substitution de X pour le cycle benzène étant

en position para,

E et Y peuvent être mutuellement identiques ou différents, et représentent un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène.

41. Composition pharmaceutique selon la revendication 40, dans laquelle, dans la formule (I'''), Q' représente un groupe de formule :

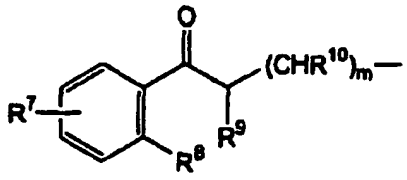


dans laquelle R^3 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle,

R^4 et R^5 sont mutuellement identiques ou différents et représentent un atome d'hydrogène ou un groupe alkyle en C_1 à C_3, ou bien R^4 et R^5 sont pris ensemble pour représenter -O-,

R^6 représente un atome d'hydrogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5, et n est un entier de 1 à 6.

42. Composition pharmaceutique selon la revendication 40, dans laquelle, dans la formule (I'''), Q' représente un groupe de formule :

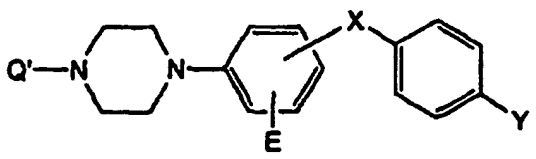


dans laquelle R^7 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle,

R^8 et R^9 sont mutuellement identiques ou différents et représentent un atome d'hydrogène ou un groupe alkyle en C_1 à C_5, ou bien R^8 et R^9 sont pris ensemble pour représenter un groupe méthylène,

R^{10} représente un atome d'hydrogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5, et m est un entier de 0 à 6.

43. Médicament pour soulager ou traiter des symptômes basés sur des maladies ischémiques ou des symptômes dérivant de crises, d'épilepsie et de migraine, contenant, à titre d'ingrédient efficace, un composé de formule (I''') ou son sel acceptable en pharmacie :



(I''')

où Q' représente un groupe de formule :

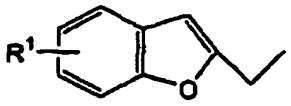
R'-A-B-

dans laquelle R' représente un groupe phényle, un groupe phénoxy ou un groupe benzoyle, chacun pouvant être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

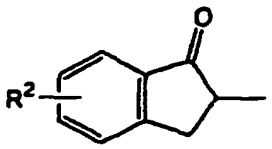
A représente une liaison de connexion, un groupe cycloalkylène en C_3 à C_6, un groupe alcénylène en C_2 à C_4 qui peut être substitué par un groupe alkyle en C_1 à C_3, un groupe di (alcoxy en C_1 à C_5)méthylène, ou un groupe hydroxyiminométhylène, et

B représente un groupe alkylène en C_1 à C_6 qui peut être substitué par un groupe hydroxyle ou un groupe alcoxy en C_1 à C_5 ;

un groupe de formule :



dans laquelle R^1 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ; ou
un groupe de formule :

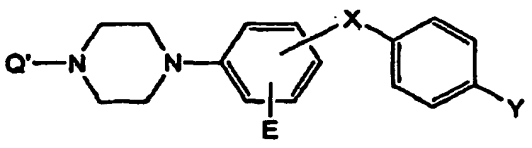


dans laquelle R^2 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ;

X représente un atome d'oxygène ou un groupe méthylène, la substitution de X pour le cycle benzène étant en position para,

E et Y peuvent être mutuellement identiques ou différents, et représentent un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène.

44. Suppresseur de surcharge en Ca^{2+} contenant, à titre d'ingrédient actif, un composé de formule (I'") ou son sel acceptable en pharmacie :



(I'")

où Q' représente un groupe de formule :

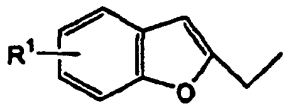
R'-A-B-

dans laquelle R' représente un groupe phényle, un groupe phénoxy ou un groupe benzoyle, chacun pouvant être substitué par un atome d'halogène, un groupe hydroxyle, un groupe alcoxy en C_1 à C_5 ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

A représente une liaison de connexion, un groupe cycloalkylène en C_3 à C_6, un groupe alcénylène en C_2 à C_4 qui peut être substitué par un groupe alkyle en C_1 à C_3, un groupe di (alcoxy en C_1 à C_5)méthylène, ou un groupe hydroxyiminométhylène, et

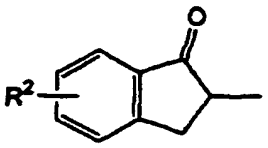
B représente un groupe alkylène en C_1 à C_6 qui peut être substitué par un groupe hydroxyle ou un groupe alcoxy en C_1 à C_5 ;

un groupe de formule :



dans laquelle R^1 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ; ou

un groupe de formule :

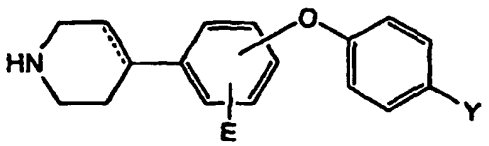


dans laquelle R^2 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe hydroxyle ;

X représente un atome d'oxygène ou un groupe méthylène, la substitution de X pour le cycle benzène étant en position para,

E et Y peuvent être mutuellement identiques ou différents, et représentent un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène.

45. Composé de formule générale (IIa) ou son sel :



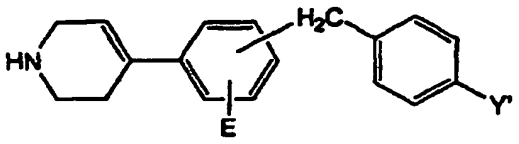
(IIa)

dans laquelle E et Y peuvent être mutuellement identiques ou différents, et représentent un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène,

la ligne de tirets montre la présence ou l'absence d'une liaison, et

la substitution du cycle benzène se liant au cycle pipéridine ou au cycle tétrahydropyridine et le groupe $-OC_6H_4Y$ est en position para.

46. Composé de formule (IIb) ou son sel :

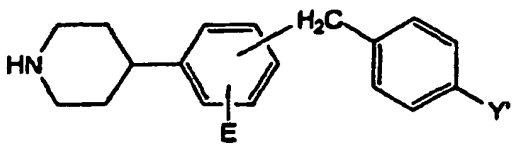


(IIb)

dans laquelle E représente un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, Y' représente un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, et

la substitution du cycle benzène se liant au cycle tétrahydropyridine et le groupe $-CH_2C6H4Y'$ est en position para.

47. Composé de formule (IIc) ou son sel :

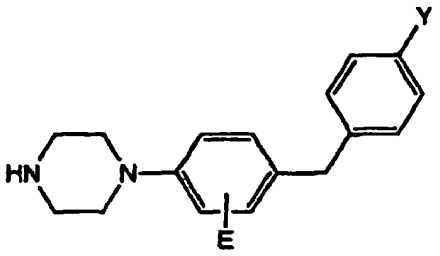


(IIc)

dans laquelle E représente un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, Y' représente un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène, et

la substitution du cycle benzène se liant au cycle pipéridine et le groupe $-CH_2C_6H_4Y'$ est en position para.

48. Composé de formule (IIIa) ou son sel :



(IIIa)

dans laquelle E et Y peuvent être mutuellement identiques ou différents, et représentent un atome d'hydrogène, un groupe hydroxyle, un atome d'halogène, un groupe alcoxy en C_1 à C_5, ou un groupe alkyle en C_1 à C_5 qui peut être substitué par un atome d'halogène.